Access DB# 74015

SEARCH REQUEST FORM

Scientific and Technical Inf rmation Center

Requester's Full Name: Billy D. Chism Examiner #: 79291 Date: 23 August 2002
Art Unit: 1653 Phone Number 30 6-5815 Serial Number: 09/767,633
Mail Box and Bldg/Room Location: _____ Results Format Preferred (circle): PAPER DISK E-MAIL
CM1 9801 / 9D12

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Methods of treating Diabetic cardiomyopathy using glycogen phosphorylase inhibitors.

Inventors (please provide full names): Judith L. Treadway (2)

Earliest Priority Filing Date: 01/24/2000 (3)

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search the attached compound (4) in conjunction with the following Key words: In particular the attached compound names. (5)

1. glycogen phosphorylase inhibitor
2. diabetic (6)
3. diabetes
4. cardiovascular
5. heart
6. ischemia (myocardial)
7. reperfusion (7)

Thank You,

Billy D. Chism

Point of Contact:
Thomas G. Larson
703-308-7309
CM1, Rm. 6 B 01

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AUG 23 2002
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Point of Contact:
Thomas G. Larson, Ph.D.
703-308-7309
CM1, Rm. 6 B 01

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STAFF USE ONLY

Searcher: Point of Contact: Thomas G. Larson, Ph.D.
Searcher Phone #: 703-308-7309
Searcher Location: CM1, Rm. 6 B 01
Date Searcher Picked Up: _____
Date Completed: 9/5
Searcher Prep & Review Time: 120
Clerical Prep Time: _____
Online Time: 330

Type of Search

NA Sequence (#) _____
AA Sequence (#) _____
Structure (#) 8
Bibliographic ✓
Litigation _____
Fulltext _____
Patent Family _____
Other _____

Vendors and cost where applicable

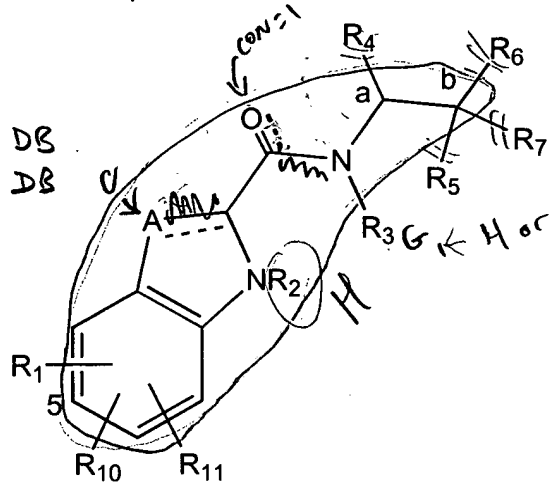
STN #1402
Dialog _____
Questel/Orbit _____
Dr.Link _____
Lexis/Nexis _____
Sequence Systems _____
WWW/Internet _____
Other (specify) _____

PTO-1590 (8-01)

Methods for making the above recited glycogen phosphorylase inhibitors of Formula A can be found in U.S. provisional patent application number 60/157,148, filed September 30, 1999.

Commonly assigned PCT published applications WO 96/39384 and WO 96/39385 disclose glycogen phosphorylase inhibitors of Formulas I and IA below that can be used to treat diabetic cardiomyopathy in accordance with the present invention.

One group of glycogen phosphorylase inhibitors that can be used in the present invention includes compounds of Formula I



Formula I

and the pharmaceutically acceptable salts and prodrugs thereof

wherein

the dotted line (---) is an optional bond;

A is -C(H)=, -C((C$_1$-C$_4$)alkyl)= or -C(halo)= when the dotted line (---) is a bond, or A is methylene or -CH((C$_1$-C$_4$)alkyl)- when the dotted line (---) is not a bond;

R$_1$, R$_{10}$ or R$_{11}$ are each independently H, halo, 4-, 6- or 7-nitro, cyano, (C$_1$-C$_4$)alkyl, (C$_1$-C$_4$)alkoxy, fluoromethyl, difluoromethyl or trifluoromethyl;

R$_2$ is H;

R$_3$ is H or (C$_1$-C$_5$)alkyl;

R$_4$ is H, methyl, ethyl, n-propyl, hydroxy(C$_1$-C$_3$)alkyl, (C$_1$-C$_3$)alkoxy(C$_1$-C$_3$)alkyl, phenyl(C$_1$-C$_4$)alkyl, phenylhydroxy(C$_1$-C$_4$)alkyl, phenyl(C$_1$-C$_4$)alkoxy(C$_1$-C$_4$)alkyl, thien-2- or -3-yl(C$_1$-C$_4$)alkyl or fur-2- or -3-yl(C$_1$-C$_4$)alkyl wherein said R$_4$ rings are mono-, di- or tri-substituted independently on carbon with H, halo, (C$_1$-C$_4$)alkyl, (C$_1$-C$_4$)alkoxy, trifluoromethyl, hydroxy, amino or cyano; or

Claims

What is claimed is:

1. A method of treating diabetic cardiomyopathy, the method comprising administering to a patient having or at risk of having diabetic cardiomyopathy a therapeutically effective amount of a glycogen phosphorylase inhibitor.

2. The method of claim 1 wherein the glycogen phosphorylase inhibitor is selected from 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxy-dimethylcarbamoyl-methyl)-2-phenyl-ethyl]-amide;

5,6-dichloro-1H-indole-2-carboxylic acid {(1S)-[(R)-hydroxy-(methoxy-methyl-carbamoyl)-methyl]-2-phenyl-ethyl}-amide;

5-chloro-1H-indole-2-carboxylic acid {(1S)-[(R)-hydroxy-(methoxy-methyl-carbamoyl)-methyl]-2-phenyl-ethyl}-amide;

5-chloro-1H-indole-2-carboxylic acid ((1S)-{(R)-hydroxy-[(2-hydroxy-ethyl)-methyl-carbamoyl]-methyl}-2-phenyl-ethyl)-amide;

5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-3-((3R,4S)-dihydroxy-pyrrolidin-1-yl)-(2R)-hydroxy-3-oxo-propyl]-amide;

5-chloro-1H-indole-2-carboxylic acid {(1S)-[(R)-hydroxy-(methyl-pyridin-2-yl-carbamoyl)-methyl]-2-phenyl-ethyl}-amide; or

5-chloro-1H-indole-2-carboxylic acid ((1S)-{(R)-hydroxy-[methyl-(2-pyridin-2-yl-ethyl)-carbamoyl]-methyl}-2-phenyl-ethyl)-amide, or a pharmaceutically acceptable salt or prodrug thereof, or a salt of a prodrug.

3. A method of treating diabetic cardiomyopathy, the method comprising administering to a patient having 1) diabetes and 2) cardiovascular disease, ischemic heart disease, congestive heart failure, congestive heart failure but not having coronary arteriosclerosis, hypertension, diastolic blood pressure abnormalities, microvascular diabetic complications, abnormal left ventricular function, myocardial fibrosis, abnormal cardiac function, pulmonary congestion, small vessel disease, small vessel disease without atherosclerotic cardiovascular disease or luminal narrowing, coagulopathy, cardiac contusion, or having had or at risk of having a myocardial infarction a therapeutically effective amount of a glycogen phosphorylase inhibitor.

Search for Species of claim 2. CAS Registry Nos. used in search were obtained from Inventors' priority documents, WO 96/39384 and WO 96/39385.


```
=> D QUE L32
L1          6031 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHORYLASE+PFT/CT OR
                 PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI
L2           465 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 (L) (INHIBIT? OR ANTAGONI?)

L3           153 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (ANTIDIABETIC AGENTS+NT,PFT/CT
                  OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR
                 PKT OR DMA)/RL
L4         47128 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DIABETES INSIPIDUS+NT,PFT/CT
                 OR DIABETES MELLITUS+NT,PFT/CT
L5           304 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HEART, DISEASE (L) DIABETIC
                 CARDIOMYOPATHY"+PFT/CT
L6        287453 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARDIOVASCULAR SYSTEM+NT,PFT/C
                 T
L7         20270 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HEART, DISEASE (L) CARDIOMYOP
                 ATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT
                 OR ISCHEMIA+NT,PFT/CT
L8          9348 SEA FILE=HCAPLUS ABB=ON  PLU=ON  REPERFUSION+PFT/CT OR
                 "REPERFUSION (L) INJURY"+PFT/CT
L9        335374 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L2 OR L3 OR L4 OR L5 OR L6
                 OR L7 OR L8)
L10            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  186392-40-5/RN
L17           10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10
L24            9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L17
L31            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  WO199639384/PN OR WO199639385/
                 PN
L32            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24 NOT L31
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claim 2, 1st compound CAS Reg. No.

— Remove inventors' priority documents from answer set.

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=> FIL REG
FILE 'REGISTRY' ENTERED AT 11:56:46 ON 05 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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COPYRIGHT (C) 2002 American Chemical Society (ACS)

STRUCTURE FILE UPDATES:    4 SEP 2002  HIGHEST RN 446821-48-3
DICTIONARY FILE UPDATES:   4 SEP 2002  HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> D L10

L10  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   186392-40-5  REGISTRY
CN   1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-
     oxo-1-(phenylmethyl)propyl]- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Indole-2-carboxamide, 5-chloro-N-[3-(dimethylamino)-2-hydroxy-3-oxo-1-
     (phenylmethyl)propyl]-, [R-(R*,S*)]-
OTHER NAMES:
```

Point of Contact:
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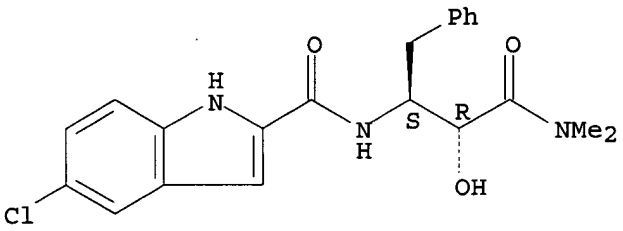
703-308-7309
CM1, Rm. 6 B 01

CN CP 91149
FS STEREOSEARCH
MF C21 H22 Cl N3 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10 REFERENCES IN FILE CA (1967 TO DATE)
10 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS
FILE 'HCAPLUS' ENTERED AT 11:57:07 ON 05 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10
FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> D IBIB AB HIT L32 1-8

Hits from CAPLUS with compound & key words

L32 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:709687 HCAPLUS
DOCUMENT NUMBER: 135:272869
TITLE: Synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes

INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136071	A2	20010926	EP 2001-301979	20010305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001302546	A2	20011031	JP 2001-78839	20010319

PRIORITY APPLN. INFO.: US 2000-191381P P 20000322
OTHER SOURCE(S): MARPAT 135:272869

AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH2, CH-alkyl when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6- or 7-NO2, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R2 = H; R3 = H, alkyl; R4 = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R5 = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R7 = H, F, alkyl; or R5 and R7 can be taken together to be oxo; R6 = carboxy, alkoxycarbonyl, amido, acyl, alkyl, OH, alkoxy; R9 = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and derivs. were prepd. Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydroxypyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF, HOBt, EDC, room temp.) to give amide II. Compds. I are glycogen phosphorylase inhibitors used for treating type 2 diabetes mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-glycogen phosphorylase inhibiting anti-diabetic agents are also claimed.

IT **Diabetes mellitus**
(non-insulin-dependent; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

IT **186392-40-5P** 186392-46-1P 186392-47-2P 186392-49-4P
186392-51-8P 186392-52-9P 186392-53-0P 186392-64-3P 186392-65-4P
186392-70-1P 186429-64-1P 186429-91-4P 186430-03-5P 186430-23-9P
186430-41-1P 186430-83-1P 186431-27-6P 186431-28-7P 186431-29-8P
225929-30-6P 251446-20-5P 251446-21-6P 251446-22-7P 251446-23-8P
251446-24-9P 251446-25-0P 251446-26-1P 251446-27-2P 251446-28-3P
251446-29-4P 251446-30-7P 251446-31-8P 251446-32-9P 251446-33-0P
251446-34-1P 251446-35-2P 332098-11-0P 332098-12-1P 332098-13-2P
332098-14-3P 332098-15-4P 332098-16-5P 332098-17-6P 332098-18-7P
332098-19-8P 332098-20-1P 332098-21-2P 332098-22-3P 332098-23-4P
332098-24-5P 332098-25-6P 332098-26-7P 332098-27-8P 332098-28-9P
332098-29-0P 332098-30-3P 332098-31-4P 332098-32-5P 332098-33-6P
332098-34-7P 332098-35-8P 332098-36-9P 332098-37-0P 332098-38-1P
332098-39-2P 332098-40-5P 332098-41-6P 332098-42-7P 332098-43-8P
332098-44-9P 332098-45-0P 332098-46-1P 332098-47-2P 332098-48-3P
332098-49-4P 332098-50-7P 332098-52-9P 332098-54-1P 332098-55-2P
332098-57-4P 332098-59-6P 332098-61-0P 332098-63-2P 332098-65-4P
362521-64-0P 362521-65-1P 362521-66-2P 362521-89-9P 362521-91-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

L32 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:693054 HCAPLUS
DOCUMENT NUMBER: 135:247221
TITLE: Pharmaceutical compositions containing glycogen phosphorylase inhibitors
INVENTOR(S): Hoover, Dennis Jay; Shanker, Ravi Mysore; Friesen, Dwayne Thomas; Lorenz, Douglas Alan; Nightingale, James Alan Schriver
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068055	A1	20010920	WO 2001-IB394	20010316
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001053778	A1	20011220	US 2001-805828	20010314

PRIORITY APPLN. INFO.: US 2000-189942P P 20000316
OTHER SOURCE(S): MARPAT 135:247221

AB Pharmaceutical compns. comprise a glycogen phosphorylase inhibitor and at least one concn.-enhancing polymer. The compn. may be a simple phys. mixt. of glycogen phosphorylase inhibitor and concn.-enhancing polymer or a dispersion of glycogen phosphorylase inhibitor and polymer. A dispersion of 25% 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3R,4S)-dihydroxypyrrolidin-1-yl)-3-oxypropyl]amide and 75% polymer was made by first mixing the drug in acetone together with HPMCAS to form a soln. The soln. comprised 1.25 drug, 3.75% HPMCAS, and 95% acetone. This soln. was then spray-dried by directing an atomizing spray using a 2-fluid external-mix spray nozzle at 2.6 bar at a feed rate of 175 to 180 g/min into the stainless-steel chamber of a spray-dryer, maintained at 180.degree. on the inlet and 69.degree. at the outlet. The resulting amorphous solid spray-dried dispersion was collected and then dried in a solvent tray-dryer by spreading the spray-dried particles onto polyethylene-lined trays to a depth of not >1 cm and then drying them at 40.degree. for at least 8 h.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Heart, disease**
(**diabetic cardiomyopathy**; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)
IT **Heart, disease**
(**ischemia**; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)
IT **Diabetes mellitus**
(non-insulin-dependent; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)
IT Antitumor agents

Atherosclerosis
Cataract
Digestive tract
Dissolution rate
Drug bioavailability
Hypercholesterolemia
Hyperglycemia
Hypertension
Hypertriglyceridemia
Ischemia
Solubility
Solvent effect
(pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**inhibitors**; pharmaceutical compns. contg. glycogen phosphorylase **inhibitors**)

IT **186392-40-5** 186392-43-8 186392-51-8 186392-53-0
186392-63-2 186392-65-4 186429-91-4 186430-03-5 186430-23-9
186430-40-0 186430-57-9 186431-27-6 251446-20-5 251446-21-6
251446-32-9 332098-16-5 332098-17-6 361176-31-0
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

L32 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:554794 HCAPLUS
DOCUMENT NUMBER: 135:132447
TITLE: Chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123

PRIORITY APPLN. INFO.: US 2000-177770P P 20000124

AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylmethyl)-2-phenylethyl]amide, etc., and their prodrugs are claimed as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy. The title compds. can also combine with insulin, insulin analogs (biguanides), .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma. agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors, .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid receptor antagonists, and/or thyroid hormone analogs for treatment of

diabetes, cardiovascular diseases, heart ischemia, congestive heart failure, hypertension, diabetic angiopathy, myocardial infarction, etc.

IT **Blood vessel, disease**
(diabetic angiopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(**diabetic cardiomyopathy**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Cardiovascular system**
(disease; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(failure; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**
(infarction; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**
(**ischemia**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT 56-03-1D, Biguanide, derivs. 504-75-6D, Imidazoline, derivs. 7440-62-2D, Vanadium, salts, biological studies 9004-10-8, Insulin, biological studies 97322-87-7D, TroGlitazone, derivs. 186392-21-2 186392-39-2 **186392-40-5** 186392-49-4 186392-65-4 186392-67-6 186392-70-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase **inhibitors** for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

L32 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:566034 HCAPLUS
DOCUMENT NUMBER: 131:199699
TITLE: N-[(Substituted five-membered di- or triaza diunsaturated ring)carbonyl]guanidine derivatives for the treatment of ischemia
INVENTOR(S): Hamanaka, Ernest S.; Guzman-Perez, Angel; Ruggeri, Roger B.; Wester, Ronald T.; Mularski, Christian J.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 246 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943663	A1	19990902	WO 1999-IB206	19990205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2321642	AA	19990902	CA 1999-2321642	19990205
AU 9920706	A1	19990915	AU 1999-20706	19990205
AU 739403	B2	20011011		
BR 9908332	A	20001107	BR 1999-8332	19990205
EP 1056729	A1	20001206	EP 1999-901083	19990205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002504546	T2	20020212	JP 2000-533420	19990205
ZA 9901578	A	20000828	ZA 1999-1578	19990226
NO 2000004192	A	20000822	NO 2000-4192	20000822

PRIORITY APPLN. INFO.: US 1998-76362P P 19980227
WO 1999-IB206 W 19990205

OTHER SOURCE(S): MARPAT 131:199699

AB Guanidine derivs. ZCON:C(NH2)2 [I; Z = certain (un)substituted, diunsatd., diazoles and triazoles] and their pharmaceutically acceptable salts and/or prodrugs are disclosed, for use as inhibitors of sodium-hydrogen exchanger type 1 (NHE-1). Also disclosed are methods of using I, and pharmaceutical compns. contg. them. I are useful for the redn. of tissue damage resulting from tissue ischemia (no data). A large no. of compds. I and their intermediates were prepd. and/or specifically claimed. For instance, guanidine-HCl was converted to the free base, taken up in THF-DMF mixt., and coupled with 5-methyl-2-(2-methoxyphenyl)-2H-1,2,3-triazole-4-carboxylic acid (pre-activated with carbonyldiimidazole), and the resultant guanidine deriv. was isolated and acidified with HCl in MeOH, to give title compd. II.HCl in 17% yield.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Brain, disease
Heart, disease
Intestine, disease
Kidney, disease
Liver, disease
Lung, disease
Muscle, disease
Pancreas, disease
Spleen
(**ischemia**; prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of **ischemia**)

IT **Ischemia**
(prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of ischemia)

IT 9028-31-3, Aldose reductase **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(pharmaceuticals also contg. **inhibitors** of; prepn. of diazole and triazole guanidine derivs. as NHE-1 **inhibitors** for

treatment of ischemia)

IT 110703-94-1, 3,4-Dihydro-4-oxo-3-[[5-(trifluoromethyl)-2-benzothiazolyl]methyl]-1-phthalazineacetic acid **186392-40-5**
186392-43-8 186392-49-4 186392-53-0 186392-64-3 186392-65-4
186429-64-1 186429-78-7 186429-91-4 186430-03-5 186430-23-9
186430-41-1 186430-57-9 186431-27-6 225929-30-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg.; prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of ischemia)

L32 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:354425 HCAPLUS
DOCUMENT NUMBER: 131:9635
TITLE: Combination of an aldose reductase inhibitor and a glycogen phosphorylase inhibitor
INVENTOR(S): Mylari, Banavara Lakshman; Hoover, Dennis Jay; Hulin, Bernard; Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926659	A1	19990603	WO 1998-IB1752	19981102
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2310069	AA	19990603	CA 1998-2310069	19981102
AU 9895558	A1	19990615	AU 1998-95558	19981102
AU 733304	B2	20010510		
EP 1032424	A1	20000906	EP 1998-949193	19981102
EP 1032424	B1	20010912		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9814698	A	20001003	BR 1998-14698	19981102
AT 205403	E	20010915	AT 1998-949193	19981102
ES 2161548	T3	20011201	ES 1998-949193	19981102
JP 2002504478	T2	20020212	JP 2000-521860	19981102
ZA 9810636	A	20000522	ZA 1998-10636	19981120
NO 2000002164	A	20000719	NO 2000-2164	20000427

PRIORITY APPLN. INFO.: US 1997-66365P P 19971121
WO 1998-IB1752 W 19981102

AB Pharmaceutical compns., kits and methods comprising combination of aldose reductase inhibitors (0.1-20 mg/kg) and glycogen phosphorylase inhibitors (0.1-15 mg/kg), useful for treatment of insulin resistant conditions such as diabetes, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis, and tissue ischemia, etc., are described. E.g., a tablet formulation contained an active ingredient (an aldose reductase inhibitor, a glycogen phosphorylase inhibitor, or a combination of the two) 0.25-100, starch 45, microcryst. cellulose 35, PVP (as 10% soln. in water) 4, Na CM-cellulose 4.5, Mg stearate 0.5, and talc 1 mg/tablet, resp.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Acromegaly
Anti-infective agents
Anti-ischemic agents
Anticholesteremic agents
Antidiabetic agents
Antihypertensives
Antiobesity agents
Brain, disease
Cardiovascular agents
Drug delivery systems
Heart, disease
Hypolipemic agents
Kidney, disease
Liver, disease
Lung, disease
Muscle, disease
Pancreas, disease
Pregnancy
Spleen, disease
(compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT **Diabetes mellitus**
(non-insulin-dependent; compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT **Heart**
(surgery; compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT 110703-94-1 **186392-40-5** 186392-43-8 186392-49-4
186392-53-0 186392-64-3 186429-64-1 186429-78-7 186430-11-5
186430-23-9 186430-41-1 186430-52-4 186431-27-6 208830-24-4
208830-25-5 225929-30-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT 9028-31-3, Aldose reductase **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(compns. for **inhibitors** of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

L32 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:450920 HCAPLUS
DOCUMENT NUMBER: 129:189205
TITLE: Indole-2-carboxamide inhibitors of human liver glycogen phosphorylase
AUTHOR(S): Hoover, Dennis J.; Lefkowitz-Snow, Sheri; Burgess-Henry, Jana L.; Martin, William H.; Armento, Sandra J.; Stock, Ingrid A.; McPherson, R. Kirk; Genereux, Paul E.; Gibbs, E. Michael; Treadway, Judith L.
CORPORATE SOURCE: Department of Cardiovascular and Metabolic Diseases Medicinal Chemistry, Central Research Division, Pfizer Inc., Groton, CT, 06340, USA

SOURCE: Journal of Medicinal Chemistry (1998), 41(16), 2934-2938
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Indole-2-carboxamide derivs. (I; X = Cl, F, Br, H, OMe; R = Ph, cyclohexyl, H, F; Y = CONMe2, CONHMe, CO2Me, CO2H, CH2OH, CONH2, etc.) were prepd. I are potent inhibitors of human liver glycogen phosphorylase which are active in cells, and produce hypoglycemic activity on oral administration in a rodent model of type 2 diabetes. I [CP-320626; X = Cl, R = F, Y = CO(1-piperidin-4-ol)] produced oral activity at 10 mg/kg.

IT **Diabetes mellitus**
(non-insulin-dependent; indole-2-carboxamide inhibitors of human liver glycogen phosphorylase)

IT **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(human liver; indole-2-carboxamide **inhibitors** of human liver glycogen phosphorylase)

IT 17186-56-0P 78800-68-7P 109522-21-6P 111258-71-0P 111321-55-2P
123665-42-9P 186392-10-9P 186392-11-0P 186392-12-1P 186392-13-2P
186392-22-3P 186392-32-5P 186392-33-6P 186392-34-7P 186392-38-1P
186392-40-5P 186392-56-3P 186429-59-4P 186429-60-7P
186430-05-7P 186430-23-9P 186430-32-0P 186430-34-2P 186430-36-4P
186430-37-5P 186430-39-7P 186430-44-4P 186431-50-5P 186431-51-6P
186431-67-4P 186431-68-5P 186432-24-6P 186432-25-7P 186432-26-8P
211677-10-0P 211677-11-1P 211677-12-2P 211677-13-3P 211677-14-4P
211677-15-5P 211677-16-6P 211677-17-7P 211677-18-8P 211677-19-9P
211677-20-2P 211677-21-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indole-2-carboxamide inhibitors of human liver glycogen phosphorylase)

L32 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:388320 HCAPLUS
DOCUMENT NUMBER: 129:72196
TITLE: Use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia
INVENTOR(S): Hoover, Dennis J.; Martin, William Holt; Tracey, Wayne Ross; Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 52 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 846464	A2	19980610	EP 1997-309727	19971203
EP 846464	A3	19990217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 5952322	A	19990914	US 1997-978384	19971125
CA 2223317	AA	19980605	CA 1997-2223317	19971203
JP 10194990	A2	19980728	JP 1997-332523	19971203
JP 3277147	B2	20020422		

AU 9746869 A1 19980611 AU 1997-46869 19971204
AU 717547 B2 20000330
ZA 9710907 A 19990604 ZA 1997-10907 19971204
PRIORITY APPLN. INFO.: US 1996-31584P P 19961205
OTHER SOURCE(S): MARPAT 129:72196

AB The use of a glycogen phosphorylase inhibitor for the manuf. of a medicament for reducing non-cardiac tissue damage resulting from ischemia or hypoxia. The tissue is brain, liver, kidney, lung, gut, skeletal muscle, spleen, pancreas, nerve, spinal code, retina tissue, the vasculature or intestinal tissue. Said glycogen phosphorylase inhibitor is represented by a compd. of formula [I; A = C(X): (wherein X = H, C1-4 alkyl, halo) when the dotted line is a bond; A = CH2 or CH(C1-4 alkyl) when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6-, or 7-NO2, cyano, C1-4 alkyl or alkoxy, CH2F, CF2H, CF3; R2 = H; R3 = H, C1-5 alkyl; R4 = H, Me, Et, n-Pr, C1-3 hydroxyalkyl, C1-3 alkoxy-C1-3 alkyl, phenyl-C1-4 alkyl, thien-2- or -3-yl-C1-4 alkyl, furan-2- or -3-yl-C1-4 alkyl, etc.; R5 = H, OH, F, C1-5 alkyl or alkoxy, C1-6 alkanoyl, amino-C1-4 alkoxy, mono-N- or di-N, N-C1-4 alkyl amino-C1-4 alkoxy, carboxy-C1-4 alkoxy, etc.; R7 = H, F, C1-5 alkyl; or R5 and R7 are taken together to form oxo; R6 = CO2H, C1-8 alkoxycarbonyl, (un)substituted CONH2, COR12; wherein R12 = piperazin-1-yl, 4-(C1-4 alkyl)piperazin-1-yl, 4-formylpiperazin-1-yl, morpholino, thiomorpholino, 1-oxothiomorpholino, 1,1-dioxothiomorpholino, thizolidin-3-yl, etc.], e.g. indolecarboxamide (II) which inhibited human liver glycogen phosphorylase a (HLGPa) and human muscle glycogen phosphorylase a (HMGPa) with IC50 of 45 and 85 nM, resp.

IT **Blood vessel, disease**
Brain, disease
Intestine, disease
Intestine, disease
Kidney, disease
Liver, disease
Lung, disease
Nerve, disease
Pancreas, disease
Pancreas, disease
Spinal cord
(injury; use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from **ischemia** or hypoxia)

IT Animal tissue
Digestive tract
Hypoxia, animal
Ischemia
Spleen
(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

IT **186392-40-5** 186392-43-8 186392-46-1 186392-49-4
186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9
186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

IT **186392-40-5** 186392-43-8 186392-46-1 186392-49-4
186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9
186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

L32 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:121995 HCAPLUS
DOCUMENT NUMBER: 128:252809
TITLE: Discovery of a human liver glycogen phosphorylase inhibitor that lowers blood glucose in vivo
AUTHOR(S): Martin, William H.; Hoover, Dennis J.; Armento, Sandra J.; Stock, Ingrid A.; Mcpherson, R. Kirk; Danley, Dennis E.; Stevenson, Ralph W.; Barrett, Eugene J.; Treadway, Judith L.
CORPORATE SOURCE: Central Research Division, Department of Exploratory Medicinal Biology, Pfizer, Inc, Groton, CT, 06340, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(4), 1776-1781
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An inhibitor of human liver glycogen phosphorylase a (HLGPa) has been identified and characterized in vitro and in vivo. This substance, [R-(R*,S*)]-5-chloro-N-[3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-1H-indole-2-carboxamide (CP-91149), inhibited HLGPa with an IC50 of 0.13 .mu.M in the presence of 7.5 mM glucose. CP-91149 resembles caffeine, a known allosteric phosphorylase inhibitor, in that it is 5- to 10-fold less potent in the absence of glucose. Further anal., however, suggests that CP-91149 and caffeine are kinetically distinct. Functionally, CP-91149 inhibited glucagon-stimulated glycogenolysis in isolated rat hepatocytes ($P < 0.05$ at 10-100 .mu.M) and in primary human hepatocytes (2.1 .mu.M IC50). In vivo, oral administration of CP-91149 to diabetic ob/ob mice at 25-50 mg/kg resulted in rapid (3 h) glucose lowering by 100-120 mg/dL ($P < 0.001$) without producing hypoglycemia. Further, CP-91149 treatment did not lower glucose levels in normoglycemic, nondiabetic mice. In ob/ob mice pretreated with 14C-glucose to label liver glycogen, CP-91149 administration reduced 14C-glycogen breakdown, confirming that glucose lowering resulted from inhibition of glycogenolysis in vivo. These findings support the use of CP-91149 in investigating glycogenolytic vs. gluconeogenic flux in hepatic glucose prodn., and they demonstrate that glycogenolysis inhibitors may be useful in the treatment of type 2 diabetes.

IT **Diabetes mellitus**
(non-insulin-dependent; blood glucose lowering by CP-91149, oral inhibitor of human liver glycogen phosphorylase, in model of type II diabetes)

IT **186392-40-5P**, CP 91149
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(blood glucose lowering by CP-91149, oral inhibitor of human liver glycogen phosphorylase, in model of type II diabetes)

=> FIL STNGUIDE
FILE 'STNGUIDE' ENTERED AT 11:58:20 ON 05 SEP 2002

FILE CONTAINS CURRENT INFORMATION.

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LAST RELOADED: Aug 30, 2002 (20020830/UP).

=> D QUE L33
L1          6031 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHORYLASE+PFT/CT OR
                 PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI
L2           465 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 (L) (INHIBIT? OR ANTAGONI?)

L3           153 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (ANTIDIABETIC AGENTS+NT,PFT/CT
                  OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR
                 PKT OR DMA)/RL
L4         47128 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DIABETES INSIPIDUS+NT,PFT/CT
                 OR DIABETES MELLITUS+NT,PFT/CT
L5           304 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HEART, DISEASE (L) DIABETIC
                 CARDIOMYOPATHY"+PFT/CT
L6        287453 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARDIOVASCULAR SYSTEM+NT,PFT/C
                 T
L7         20270 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HEART, DISEASE (L) CARDIOMYOP
                 ATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT
                 OR ISCHEMIA+NT,PFT/CT
L8           9348 SEA FILE=HCAPLUS ABB=ON  PLU=ON  REPERFUSION+PFT/CT OR
                 "REPERFUSION (L) INJURY"+PFT/CT
L9        335374 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L2 OR L3 OR L4 OR L5 OR L6
                 OR L7 OR L8)
L11            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  186392-39-2/RN   claim 2, 2nd compound
L18            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11                reg #
L25            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L18
L31            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  WO199639384/PN OR WO199639385/
                 PN
L33            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 NOT L31


=> FIL REG
FILE 'REGISTRY' ENTERED AT 11:58:51 ON 05 SEP 2002
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STRUCTURE FILE UPDATES:    4 SEP 2002  HIGHEST RN 446821-48-3
DICTIONARY FILE UPDATES:   4 SEP 2002  HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

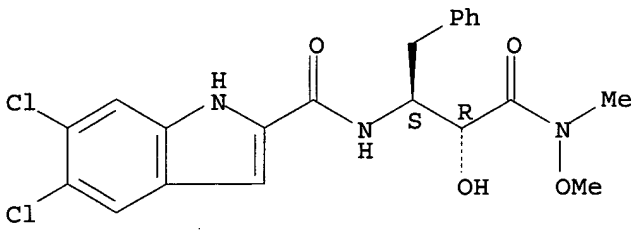
Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> D L11

L11  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   186392-39-2  REGISTRY
CN   1H-Indole-2-carboxamide, 5,6-dichloro-N-[(1S,2R)-2-hydroxy-3-
     (methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]-  (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Indole-2-carboxamide, 5,6-dichloro-N-[2-hydroxy-3-(methoxymethylamino)-
```

3-oxo-1-(phenylmethyl)propyl]-, [R-(R*,S*)]-
FS STEREOSEARCH
MF C21 H21 Cl2 N3 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS
FILE 'HCAPLUS' ENTERED AT 12:00:12 ON 05 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10
FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> D IBIB AB HIT L33

Hits in CAPLUS having key words & compound.

L33 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:554794 HCAPLUS
DOCUMENT NUMBER: 135:132447
TITLE: Chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for

treatment of diabetic cardiomyopathy
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123

PRIORITY APPLN. INFO.: US 2000-177770P P 20000124

AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylmethyl)-2-phenylethyl]amide, etc., and their prodrugs are claimed as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy. The title compds. can also combine with insulin, insulin analogs (biguanides), .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma. agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors, .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid receptor antagonists, and/or thyroid hormone analogs for treatment of diabetes, cardiovascular diseases, heart ischemia, congestive heart failure, hypertension, diabetic angiopathy, myocardial infarction, etc.

IT **Blood vessel, disease**
(diabetic angiopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(**diabetic cardiomyopathy**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Cardiovascular system**
(disease; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(failure; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**
(infarction; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**
(**ischemia**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT 56-03-1D, Biguanide, derivs. 504-75-6D, Imidazoline, derivs. 7440-62-2D, Vanadium, salts, biological studies 9004-10-8, Insulin, biological studies 97322-87-7D, TroGlitazone, derivs. 186392-21-2

186392-39-2 186392-40-5 186392-49-4 186392-65-4
186392-67-6 186392-70-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase **inhibitors** for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

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=> FIL STNGUIDE
FILE 'STNGUIDE' ENTERED AT 12:00:31 ON 05 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Aug 30, 2002 (20020830/UP).

=> D QUE L34
L1          6031 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHORYLASE+PFT/CT OR
                 PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI
L2           465 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 (L) (INHIBIT? OR ANTAGONI?)

L3           153 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (ANTIDIABETIC AGENTS+NT,PFT/CT
                  OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR
                 PKT OR DMA)/RL
L4         47128 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DIABETES INSIPIDUS+NT,PFT/CT
                 OR DIABETES MELLITUS+NT,PFT/CT
L5           304 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HEART, DISEASE (L) DIABETIC
                 CARDIOMYOPATHY"+PFT/CT
L6        287453 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARDIOVASCULAR SYSTEM+NT,PFT/C
                 T
L7         20270 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HEART, DISEASE (L) CARDIOMYOP
                 ATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT
                 OR ISCHEMIA+NT,PFT/CT
L8           9348 SEA FILE=HCAPLUS ABB=ON  PLU=ON  REPERFUSION+PFT/CT OR
                 "REPERFUSION (L) INJURY"+PFT/CT
L9        335374 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L2 OR L3 OR L4 OR L5 OR L6
                 OR L7 OR L8)
L12            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  186392-43-8/RN   claim 2, 3rd compound
L19            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12
L26            6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L19
L31            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  WO199639384/PN OR WO199639385/
                 PN
L34            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 NOT L31


=> FIL REG
FILE 'REGISTRY' ENTERED AT 12:02:03 ON 05 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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COPYRIGHT (C) 2002 American Chemical Society (ACS)
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STRUCTURE FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3
DICTIONARY FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

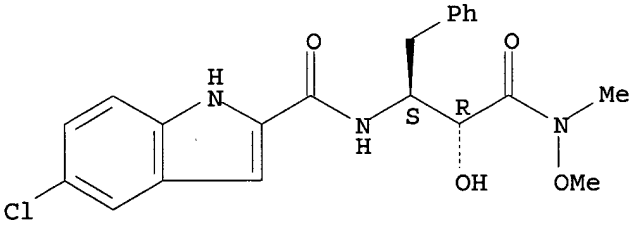
Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> D L12

L12 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **186392-43-8** REGISTRY
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]-, [R-(R*,S*)]-
FS STEREOSEARCH
MF C21 H22 Cl N3 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS
FILE 'HCAPLUS' ENTERED AT 12:02:21 ON 05 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10
FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> D IBIB AB HIT L34 1-5 Hits In CAPLUS

L34 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:693054 HCAPLUS
DOCUMENT NUMBER: 135:247221
TITLE: Pharmaceutical compositions containing glycogen phosphorylase inhibitors
INVENTOR(S): Hoover, Dennis Jay; Shanker, Ravi Mysore; Friesen, Dwayne Thomas; Lorenz, Douglas Alan; Nightingale, James Alan Schriver
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068055	A1	20010920	WO 2001-IB394	20010316
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001053778	A1	20011220	US 2001-805828	20010314

PRIORITY APPLN. INFO.: US 2000-189942P P 20000316
OTHER SOURCE(S): MARPAT 135:247221

AB Pharmaceutical compns. comprise a glycogen phosphorylase inhibitor and at least one concn.-enhancing polymer. The compn. may be a simple phys. mixt. of glycogen phosphorylase inhibitor and concn.-enhancing polymer or a dispersion of glycogen phosphorylase inhibitor and polymer. A dispersion of 25% 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3R,4S)-dihydroxypyrrolidin-1-yl)-3-oxypropyl]amide and 75% polymer was made by first mixing the drug in acetone together with HPMCAS to form a soln. The soln. comprised 1.25 drug, 3.75% HPMCAS, and 95% acetone. This soln. was then spray-dried by directing an atomizing spray using a 2-fluid external-mix spray nozzle at 2.6 bar at a feed rate of 175 to 180 g/min into the stainless-steel

chamber of a spray-dryer, maintained at 180.degree. on the inlet and 69.degree. at the outlet. The resulting amorphous solid spray-dried dispersion was collected and then dried in a solvent tray-dryer by spreading the spray-dried particles onto polyethylene-lined trays to a depth of not >1 cm and then drying them at 40.degree. for at least 8 h.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Heart, disease**
(**diabetic cardiomyopathy**; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT **Heart, disease**
(**ischemia**; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT **Diabetes mellitus**
(non-insulin-dependent; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT Antitumor agents
Atherosclerosis
Cataract
Digestive tract
Dissolution rate
Drug bioavailability
Hypercholesterolemia
Hyperglycemia
Hypertension
Hypertriglyceridemia
Ischemia
Solubility
Solvent effect
(pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**inhibitors**; pharmaceutical compns. contg. glycogen phosphorylase **inhibitors**)

IT 186392-40-5 **186392-43-8** 186392-51-8 186392-53-0
186392-63-2 186392-65-4 186429-91-4 186430-03-5 186430-23-9
186430-40-0 186430-57-9 186431-27-6 251446-20-5 251446-21-6
251446-32-9 332098-16-5 332098-17-6 361176-31-0
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

L34 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:566034 HCAPLUS
DOCUMENT NUMBER: 131:199699
TITLE: N-[(Substituted five-membered di- or triaza diunsaturated ring)carbonyl]guanidine derivatives for the treatment of ischemia
INVENTOR(S): Hamanaka, Ernest S.; Guzman-Perez, Angel; Ruggeri, Roger B.; Wester, Ronald T.; Mularski, Christian J.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 246 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 9943663	A1	19990902	WO 1999-IB206	19990205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2321642	AA	19990902	CA 1999-2321642	19990205
AU 9920706	A1	19990915	AU 1999-20706	19990205
AU 739403	B2	20011011		
BR 9908332	A	20001107	BR 1999-8332	19990205
EP 1056729	A1	20001206	EP 1999-901083	19990205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002504546	T2	20020212	JP 2000-533420	19990205
ZA 9901578	A	20000828	ZA 1999-1578	19990226
NO 2000004192	A	20000822	NO 2000-4192	20000822

PRIORITY APPLN. INFO.: US 1998-76362P P 19980227
WO 1999-IB206 W 19990205

OTHER SOURCE(S): MARPAT 131:199699

AB Guanidine derivs. ZCON:C(NH2)2 [I; Z = certain (un)substituted, diunsatd., diazoles and triazoles] and their pharmaceutically acceptable salts and/or prodrugs are disclosed, for use as inhibitors of sodium-hydrogen exchanger type 1 (NHE-1). Also disclosed are methods of using I, and pharmaceutical compns. contg. them. I are useful for the redn. of tissue damage resulting from tissue ischemia (no data). A large no. of compds. I and their intermediates were prepd. and/or specifically claimed. For instance, guanidine-HCl was converted to the free base, taken up in THF-DMF mixt., and coupled with 5-methyl-2-(2-methoxyphenyl)-2H-1,2,3-triazole-4-carboxylic acid (pre-activated with carbonyldiimidazole), and the resultant guanidine deriv. was isolated and acidified with HCl in MeOH, to give title compd. II.HCl in 17% yield.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Brain, disease
Heart, disease
Intestine, disease
Kidney, disease
Liver, disease
Lung, disease
Muscle, disease
Pancreas, disease
Spleen
(**ischemia**; prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of **ischemia**)

IT **Ischemia**
(prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of ischemia)

IT 9028-31-3, Aldose reductase **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(pharmaceuticals also contg. **inhibitors** of; prepn. of diazole and triazole guanidine derivs. as NHE-1 **inhibitors** for treatment of ischemia)

IT 110703-94-1, 3,4-Dihydro-4-oxo-3-[[5-(trifluoromethyl)-2-benzothiazolyl]methyl]-1-phthalazineacetic acid 186392-40-5

186392-43-8 186392-49-4 186392-53-0 186392-64-3
186392-65-4 186429-64-1 186429-78-7 186429-91-4 186430-03-5
186430-23-9 186430-41-1 186430-57-9 186431-27-6 225929-30-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg.; prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of ischemia)

L34 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:354425 HCAPLUS
DOCUMENT NUMBER: 131:9635
TITLE: Combination of an aldose reductase inhibitor and a glycogen phosphorylase inhibitor
INVENTOR(S): Mylari, Banavara Lakshman; Hoover, Dennis Jay; Hulin, Bernard; Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926659	A1	19990603	WO 1998-IB1752	19981102
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2310069	AA	19990603	CA 1998-2310069	19981102
AU 9895558	A1	19990615	AU 1998-95558	19981102
AU 733304	B2	20010510		
EP 1032424	A1	20000906	EP 1998-949193	19981102
EP 1032424	B1	20010912		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9814698	A	20001003	BR 1998-14698	19981102
AT 205403	E	20010915	AT 1998-949193	19981102
ES 2161548	T3	20011201	ES 1998-949193	19981102
JP 2002504478	T2	20020212	JP 2000-521860	19981102
ZA 9810636	A	20000522	ZA 1998-10636	19981120
NO 2000002164	A	20000719	NO 2000-2164	20000427

PRIORITY APPLN. INFO.: US 1997-66365P P 19971121
WO 1998-IB1752 W 19981102

AB Pharmaceutical compns., kits and methods comprising combination of aldose reductase inhibitors (0.1-20 mg/kg) and glycogen phosphorylase inhibitors (0.1-15 mg/kg), useful for treatment of insulin resistant conditions such as diabetes, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis, and tissue ischemia, etc., are described. E.g., a tablet formulation contained an active ingredient (an aldose reductase inhibitor, a glycogen phosphorylase inhibitor, or a combination of the two) 0.25-100, starch 45, microcryst. cellulose 35, PVP (as 10% soln. in water) 4, Na CM-cellulose 4.5, Mg stearate 0.5, and talc 1 mg/tablet, resp.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Acromegaly

Anti-infective agents
Anti-ischemic agents
Anticholesteremic agents
Antidiabetic agents
Antihypertensives
Antiobesity agents
Brain, disease
Cardiovascular agents
Drug delivery systems
Heart, disease
Hypolipemic agents
Kidney, disease
Liver, disease
Lung, disease
Muscle, disease
Pancreas, disease
Pregnancy
Spleen, disease
(compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT **Diabetes mellitus**
(non-insulin-dependent; compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT **Heart**
(surgery; compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT 110703-94-1 186392-40-5 **186392-43-8** 186392-49-4
186392-53-0 186392-64-3 186429-64-1 186429-78-7 186430-11-5
186430-23-9 186430-41-1 186430-52-4 186431-27-6 208830-24-4
208830-25-5 225929-30-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT 9028-31-3, Aldose reductase **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(compns. for **inhibitors** of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

L34 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:193899 HCAPLUS
DOCUMENT NUMBER: 130:227741
TITLE: Solid pharmaceutical dispersions with enhanced bioavailability
INVENTOR(S): Curatolo, William John; Herbig, Scott Max; Nightingale, James Alan Schriver
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 46 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 901786	A2	19990317	EP 1998-305960	19980727
EP 901786	A3	20000119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1207896	A	19990217	CN 1998-116282	19980810
JP 11116502	A2	19990427	JP 1998-227328	19980811
JP 2984661	B2	19991129		
BR 9803144	A	20000111	BR 1998-3144	19980811
US 2002009494	A1	20020124	US 2001-770562	20010126
PRIORITY APPLN. INFO.:			US 1997-55221P P	19970811
			US 1998-131019 B1	19980807

AB Spray dried solid dispersions comprising a sparingly sol. drug and hydroxypropyl Me cellulose acetate succinate (HPMCAS) provide increased aq. soly. and/or bioavailability in a use environment. Spray dried compns. were prepd. from HPMCAS and compds. such as ziprasidone, griseofulvin, nifedipine and phenytoin.

IT 9015-71-8, Corticotropin releasing hormone **9035-74-9**, Glycogen phosphorylase 80619-02-9, 5-Lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study) (**inhibitors**; solid pharmaceutical dispersions with enhanced bioavailability)

IT 57-41-0, Phenytoin 126-07-8, Griseofulvin 21829-25-4, Nifedipine 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate 146939-27-7, Ziprasidone 175139-41-0 175140-00-8 **186392-43-8** 186392-65-4 221163-46-8
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (solid pharmaceutical dispersions with enhanced bioavailability)

L34 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:388320 HCAPLUS
DOCUMENT NUMBER: 129:72196
TITLE: Use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia
INVENTOR(S): Hoover, Dennis J.; Martin, William Holt; Tracey, Wayne Ross; Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 52 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 846464	A2	19980610	EP 1997-309727	19971203
EP 846464	A3	19990217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 5952322	A	19990914	US 1997-978384	19971125
CA 2223317	AA	19980605	CA 1997-2223317	19971203
JP 10194990	A2	19980728	JP 1997-332523	19971203
JP 3277147	B2	20020422		
AU 9746869	A1	19980611	AU 1997-46869	19971204
AU 717547	B2	20000330		
ZA 9710907	A	19990604	ZA 1997-10907	19971204
PRIORITY APPLN. INFO.:			US 1996-31584P P	19961205
OTHER SOURCE(S):		MARPAT 129:72196		

AB The use of a glycogen phosphorylase inhibitor for the manuf. of a medicament for reducing non-cardiac tissue damage resulting from ischemia or hypoxia. The tissue is brain, liver, kidney, lung, gut, skeletal muscle, spleen, pancreas, nerve, spinal code, retina tissue, the vasculature or intestinal tissue. Said glycogen phosphorylase inhibitor is represented by a compd. of formula [I; A = C(X): (wherein X = H, C1-4 alkyl, halo) when the dotted line is a bond; A = CH2 or CH(C1-4 alkyl) when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6-, or 7-NO2, cyano, C1-4 alkyl or alkoxy, CH2F, CF2H, CF3; R2 = H; R3 = H, C1-5 alkyl; R4 = H, Me, Et, n-Pr, C1-3 hydroxyalkyl, C1-3 alkoxy-C1-3 alkyl, phenyl-C1-4 alkyl, thien-2- or -3-yl-C1-4 alkyl, furan-2- or -3-yl-C1-4 alkyl, etc.; R5 = H, OH, F, C1-5 alkyl or alkoxy, C1-6 alkanoyl, amino-C1-4 alkoxy, mono-N- or di-N, N-C1-4 alkyl amino-C1-4 alkoxy, carboxy-C1-4 alkoxy, etc.; R7 = H, F, C1-5 alkyl; or R5 and R7 are taken together to form oxo; R6 = CO2H, C1-8 alkoxycarbonyl, (un)substituted CONH2, COR12; wherein R12 = piperazin-1-yl, 4-(C1-4 alkyl)piperazin-1-yl, 4-formylpiperazin-1-yl, morpholino, thiomorpholino, 1-oxothiomorpholino, 1,1-dioxothiomorpholino, thizolidin-3-yl, etc.], e.g. indolecarboxamide (II) which inhibited human liver glycogen phosphorylase a (HLGPa) and human muscle glycogen phosphorylase a (HMGPa) with IC50 of 45 and 85 nM, resp.

IT **Blood vessel, disease**
Brain, disease
Intestine, disease
Intestine, disease
Kidney, disease
Liver, disease
Lung, disease
Nerve, disease
Pancreas, disease
Pancreas, disease
Spinal cord
(injury; use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from **ischemia** or hypoxia)

IT Animal tissue
Digestive tract
Hypoxia, animal
Ischemia
Spleen
(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

IT 186392-40-5 **186392-43-8** 186392-46-1 186392-49-4
186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9
186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

IT 186392-40-5 **186392-43-8** 186392-46-1 186392-49-4
186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9
186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

=> FIL STNGUIDE

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FILE 'STNGUIDE' ENTERED AT 12:04:17 ON 05 SEP 2002
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Aug 30, 2002 (20020830/UP).

=> D QUE L35
L1          6031 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHORYLASE+PFT/CT OR
                 PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI
L2           465 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 (L) (INHIBIT? OR ANTAGONI?)

L3           153 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (ANTIDIABETIC AGENTS+NT,PFT/CT
                  OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR
                 PKT OR DMA)/RL
L4         47128 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DIABETES INSIPIDUS+NT,PFT/CT
                 OR DIABETES MELLITUS+NT,PFT/CT
L5           304 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HEART, DISEASE (L) DIABETIC
                 CARDIOMYOPATHY"+PFT/CT
L6        287453 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARDIOVASCULAR SYSTEM+NT,PFT/C
                 T
L7         20270 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HEART, DISEASE (L) CARDIOMYOP
                 ATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT
                 OR ISCHEMIA+NT,PFT/CT
L8          9348 SEA FILE=HCAPLUS ABB=ON  PLU=ON  REPERFUSION+PFT/CT OR
                 "REPERFUSION (L) INJURY"+PFT/CT
L9        335374 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L2 OR L3 OR L4 OR L5 OR L6
                 OR L7 OR L8)
L13            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  186392-49-4/RN   claim 2, 4th compound
L20            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13
L27            6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L20
L31            2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  WO199639384/PN OR WO199639385/
                 PN
L35            5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 NOT L31


=> FIL REG
FILE 'REGISTRY' ENTERED AT 12:04:47 ON 05 SEP 2002
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STRUCTURE FILE UPDATES:    4 SEP 2002  HIGHEST RN 446821-48-3
DICTIONARY FILE UPDATES:   4 SEP 2002  HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

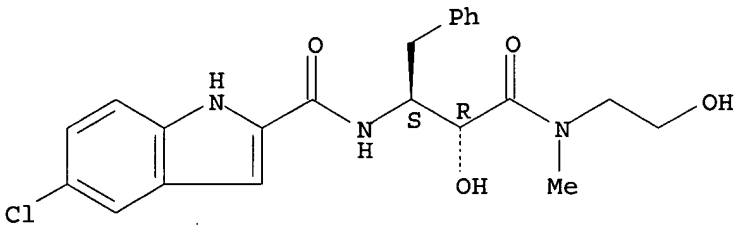
Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> D L13
```

L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **186392-49-4** REGISTRY
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(2-hydroxyethyl)methylamino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-hydroxy-3-[(2-hydroxyethyl)methylamino]-3-oxo-1-(phenylmethyl)propyl]-, [R-(R*,S*)]-
FS STEREOSEARCH
MF C22 H24 Cl N3 O4
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1967 TO DATE)
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS
FILE 'HCAPLUS' ENTERED AT 12:05:02 ON 05 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10
FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> D IBIB AB HIT L35 1-5

L35 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:709687 HCAPLUS
DOCUMENT NUMBER: 135:272869
TITLE: Synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136071	A2	20010926	EP 2001-301979	20010305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001302546	A2	20011031	JP 2001-78839	20010319

PRIORITY APPLN. INFO.: US 2000-191381P P 20000322
OTHER SOURCE(S): MARPAT 135:272869

AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH2, CH-alkyl when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6- or 7-NO2, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R2 = H; R3 = H, alkyl; R4 = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R5 = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R7 = H, F, alkyl; or R5 and R7 can be taken together to be oxo; R6 = carboxy, alkoxycarbonyl, amido, acyl, alkyl, OH, alkoxy; R9 = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and derivs. were prepd. Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydroxypyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF, HOBt, EDC, room temp.) to give amide II. Compds. I are glycogen phosphorylase inhibitors used for treating type 2 diabetes mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-glycogen phosphorylase inhibiting anti-diabetic agents are also claimed.

IT **Diabetes mellitus**
(non-insulin-dependent; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

IT 186392-40-5P 186392-46-1P 186392-47-2P **186392-49-4P**
186392-51-8P 186392-52-9P 186392-53-0P 186392-64-3P 186392-65-4P
186392-70-1P 186429-64-1P 186429-91-4P 186430-03-5P 186430-23-9P
186430-41-1P 186430-83-1P 186431-27-6P 186431-28-7P 186431-29-8P
225929-30-6P 251446-20-5P 251446-21-6P 251446-22-7P 251446-23-8P
251446-24-9P 251446-25-0P 251446-26-1P 251446-27-2P 251446-28-3P
251446-29-4P 251446-30-7P 251446-31-8P 251446-32-9P 251446-33-0P
251446-34-1P 251446-35-2P 332098-11-0P 332098-12-1P 332098-13-2P
332098-14-3P 332098-15-4P 332098-16-5P 332098-17-6P 332098-18-7P
332098-19-8P 332098-20-1P 332098-21-2P 332098-22-3P 332098-23-4P
332098-24-5P 332098-25-6P 332098-26-7P 332098-27-8P 332098-28-9P
332098-29-0P 332098-30-3P 332098-31-4P 332098-32-5P 332098-33-6P
332098-34-7P 332098-35-8P 332098-36-9P 332098-37-0P 332098-38-1P
332098-39-2P 332098-40-5P 332098-41-6P 332098-42-7P 332098-43-8P
332098-44-9P 332098-45-0P 332098-46-1P 332098-47-2P 332098-48-3P
332098-49-4P 332098-50-7P 332098-52-9P 332098-54-1P 332098-55-2P

332098-57-4P 332098-59-6P 332098-61-0P 332098-63-2P 332098-65-4P
362521-64-0P 362521-65-1P 362521-66-2P 362521-89-9P 362521-91-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

L35 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:554794 HCAPLUS
DOCUMENT NUMBER: 135:132447
TITLE: Chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123

PRIORITY APPLN. INFO.: US 2000-177770P P 20000124

AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylmethyl)-2-phenylethyl]amide, etc., and their prodrugs are claimed as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy. The title compds. can also combine with insulin, insulin analogs (biguanides), .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma. agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors, .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid receptor antagonists, and/or thyroid hormone analogs for treatment of diabetes, cardiovascular diseases, heart ischemia, congestive heart failure, hypertension, diabetic angiopathy, myocardial infarction, etc.

IT **Blood vessel, disease**
(diabetic angiopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(**diabetic cardiomyopathy**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Cardiovascular system**
(disease; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(failure; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic**

cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(infarction; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**
(**ischemia**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT 56-03-1D, Biguanide, derivs. 504-75-6D, Imidazoline, derivs. 7440-62-2D, Vanadium, salts, biological studies 9004-10-8, Insulin, biological studies 97322-87-7D, TroGlitazone, derivs. 186392-21-2 186392-39-2 186392-40-5 **186392-49-4** 186392-65-4 186392-67-6 186392-70-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase **inhibitors** for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

L35 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:566034 HCAPLUS
DOCUMENT NUMBER: 131:199699
TITLE: N-[(Substituted five-membered di- or triaza diunsaturated ring)carbonyl]guanidine derivatives for the treatment of ischemia
INVENTOR(S): Hamanaka, Ernest S.; Guzman-Perez, Angel; Ruggeri, Roger B.; Wester, Ronald T.; Mularski, Christian J.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 246 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943663	A1	19990902	WO 1999-IB206	19990205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2321642	AA	19990902	CA 1999-2321642	19990205
AU 9920706	A1	19990915	AU 1999-20706	19990205
AU 739403	B2	20011011		
BR 9908332	A	20001107	BR 1999-8332	19990205

EP 1056729 A1 20001206 EP 1999-901083 19990205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO
JP 2002504546 T2 20020212 JP 2000-533420 19990205
ZA 9901578 A 20000828 ZA 1999-1578 19990226
NO 2000004192 A 20000822 NO 2000-4192 20000822
PRIORITY APPLN. INFO.: US 1998-76362P P 19980227
WO 1999-IB206 W 19990205
OTHER SOURCE(S): MARPAT 131:199699
AB Guanidine derivs. ZCON:C(NH2)2 [I; Z = certain (un)substituted, diunsatd., diazoles and triazoles] and their pharmaceutically acceptable salts and/or prodrugs are disclosed, for use as inhibitors of sodium-hydrogen exchanger type 1 (NHE-1). Also disclosed are methods of using I, and pharmaceutical compns. contg. them. I are useful for the redn. of tissue damage resulting from tissue ischemia (no data). A large no. of compds. I and their intermediates were prepd. and/or specifically claimed. For instance, guanidine-HCl was converted to the free base, taken up in THF-DMF mixt., and coupled with 5-methyl-2-(2-methoxyphenyl)-2H-1,2,3-triazole-4-carboxylic acid (pre-activated with carbonyldiimidazole), and the resultant guanidine deriv. was isolated and acidified with HCl in MeOH, to give title compd. II.HCl in 17% yield.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT Brain, disease
Heart, disease
Intestine, disease
Kidney, disease
Liver, disease
Lung, disease
Muscle, disease
Pancreas, disease
Spleen
(**ischemia**; prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of **ischemia**)
IT **Ischemia**
(prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of ischemia)
IT 9028-31-3, Aldose reductase **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(pharmaceuticals also contg. **inhibitors** of; prepn. of diazole and triazole guanidine derivs. as NHE-1 **inhibitors** for treatment of ischemia)
IT 110703-94-1, 3,4-Dihydro-4-oxo-3-[[5-(trifluoromethyl)-2-benzothiazolyl]methyl]-1-phthalazineacetic acid 186392-40-5
186392-43-8 **186392-49-4** 186392-53-0 186392-64-3
186392-65-4 186429-64-1 186429-78-7 186429-91-4 186430-03-5
186430-23-9 186430-41-1 186430-57-9 186431-27-6 225929-30-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg.; prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of ischemia)

L35 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:354425 HCAPLUS
DOCUMENT NUMBER: 131:9635
TITLE: Combination of an aldose reductase inhibitor and a glycogen phosphorylase inhibitor
INVENTOR(S): Mylari, Banavara Lakshman; Hoover, Dennis Jay; Hulin, Bernard; Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926659	A1	19990603	WO 1998-IB1752	19981102
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2310069	AA	19990603	CA 1998-2310069	19981102
AU 9895558	A1	19990615	AU 1998-95558	19981102
AU 733304	B2	20010510		
EP 1032424	A1	20000906	EP 1998-949193	19981102
EP 1032424	B1	20010912		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9814698	A	20001003	BR 1998-14698	19981102
AT 205403	E	20010915	AT 1998-949193	19981102
ES 2161548	T3	20011201	ES 1998-949193	19981102
JP 2002504478	T2	20020212	JP 2000-521860	19981102
ZA 9810636	A	20000522	ZA 1998-10636	19981120
NO 2000002164	A	20000719	NO 2000-2164	20000427

PRIORITY APPLN. INFO.: US 1997-66365P P 19971121
WO 1998-IB1752 W 19981102

AB Pharmaceutical compns., kits and methods comprising combination of aldose reductase inhibitors (0.1-20 mg/kg) and glycogen phosphorylase inhibitors (0.1-15 mg/kg), useful for treatment of insulin resistant conditions such as diabetes, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis, and tissue ischemia, etc., are described. E.g., a tablet formulation contained an active ingredient (an aldose reductase inhibitor, a glycogen phosphorylase inhibitor, or a combination of the two) 0.25-100, starch 45, microcryst. cellulose 35, PVP (as 10% soln. in water) 4, Na CM-cellulose 4.5, Mg stearate 0.5, and talc 1 mg/tablet, resp.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Acromegaly
Anti-infective agents
Anti-ischemic agents
Anticholesteremic agents
Antidiabetic agents
Antihypertensives
Antiobesity agents
Brain, disease
Cardiovascular agents
Drug delivery systems
Heart, disease
Hypolipemic agents
Kidney, disease
Liver, disease
Lung, disease
Muscle, disease

Pancreas, disease
Pregnancy
Spleen, disease
(compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT **Diabetes mellitus**
(non-insulin-dependent; compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT **Heart**
(surgery; compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT 110703-94-1 186392-40-5 186392-43-8 **186392-49-4**
186392-53-0 186392-64-3 186429-64-1 186429-78-7 186430-11-5
186430-23-9 186430-41-1 186430-52-4 186431-27-6 208830-24-4
208830-25-5 225929-30-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT 9028-31-3, Aldose reductase **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(compns. for **inhibitors** of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

L35 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:388320 HCAPLUS
DOCUMENT NUMBER: 129:72196
TITLE: Use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia
INVENTOR(S): Hoover, Dennis J.; Martin, William Holt; Tracey, Wayne Ross; Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 52 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 846464	A2	19980610	EP 1997-309727	19971203
EP 846464	A3	19990217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 5952322	A	19990914	US 1997-978384	19971125
CA 2223317	AA	19980605	CA 1997-2223317	19971203
JP 10194990	A2	19980728	JP 1997-332523	19971203
JP 3277147	B2	20020422		
AU 9746869	A1	19980611	AU 1997-46869	19971204
AU 717547	B2	20000330		
ZA 9710907	A	19990604	ZA 1997-10907	19971204

PRIORITY APPLN. INFO.: US 1996-31584P P 19961205
OTHER SOURCE(S): MARPAT 129:72196
AB The use of a glycogen phosphorylase inhibitor for the manuf. of a

medicament for reducing non-cardiac tissue damage resulting from ischemia or hypoxia. The tissue is brain, liver, kidney, lung, gut, skeletal muscle, spleen, pancreas, nerve, spinal code, retina tissue, the vasculature or intestinal tissue. Said glycogen phosphorylase inhibitor is represented by a compd. of formula [I; A = C(X): (wherein X = H, C1-4 alkyl, halo) when the dotted line is a bond; A = CH2 or CH(C1-4 alkyl) when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6-, or 7-NO2, cyano, C1-4 alkyl or alkoxy, CH2F, CF2H, CF3; R2 = H; R3 = H, C1-5 alkyl; R4 = H, Me, Et, n-Pr, C1-3 hydroxyalkyl, C1-3 alkoxy-C1-3 alkyl, phenyl-C1-4 alkyl, thien-2- or -3-yl-C1-4 alkyl, furan-2- or -3-yl-C1-4 alkyl, etc.; R5 = H, OH, F, C1-5 alkyl or alkoxy, C1-6 alkanoyl, amino-C1-4 alkoxy, mono-N- or di-N, N-C1-4 alkyl amino-C1-4 alkoxy, carboxy-C1-4 alkoxy, etc.; R7 = H, F, C1-5 alkyl; or R5 and R7 are taken together to form oxo; R6 = CO2H, C1-8 alkoxycarbonyl, (un)substituted CONH2, COR12; wherein R12 = piperazin-1-yl, 4-(C1-4 alkyl)piperazin-1-yl, 4-formylpiperazin-1-yl, morpholino, thiomorpholino, 1-oxothiomorpholino, 1,1-dioxothiomorpholino, thizolidin-3-yl, etc.], e.g. indolecarboxamide (II) which inhibited human liver glycogen phosphorylase a (HLGPa) and human muscle glycogen phosphorylase a (HMGPa) with IC50 of 45 and 85 nM, resp.

IT **Blood vessel, disease**
Brain, disease
Intestine, disease
Intestine, disease
Kidney, disease
Liver, disease
Lung, disease
Nerve, disease
Pancreas, disease
Pancreas, disease
Spinal cord
(injury; use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from **ischemia** or hypoxia)

IT Animal tissue
Digestive tract
Hypoxia, animal
Ischemia
Spleen
(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

IT 186392-40-5 186392-43-8 186392-46-1 **186392-49-4**
186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9
186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

IT 186392-40-5 186392-43-8 186392-46-1 **186392-49-4**
186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9
186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

=> FIL STNGUIDE
FILE 'STNGUIDE' ENTERED AT 12:07:02 ON 05 SEP 2002

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Aug 30, 2002 (20020830/UP).

=> D QUE L36

L1	6031	SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHORYLASE+PFT/CT OR PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI
L2	465	SEA FILE=HCAPLUS ABB=ON PLU=ON L1 (L) (INHIBIT? OR ANTAGONI?)
L3	153	SEA FILE=HCAPLUS ABB=ON PLU=ON (ANTIDIABETIC AGENTS+NT,PFT/CT OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR PKT OR DMA)/RL
L4	47128	SEA FILE=HCAPLUS ABB=ON PLU=ON DIABETES INSIPIDUS+NT,PFT/CT OR DIABETES MELLITUS+NT,PFT/CT
L5	304	SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) DIABETIC CARDIOMYOPATHY"+PFT/CT
L6	287453	SEA FILE=HCAPLUS ABB=ON PLU=ON CARDIOVASCULAR SYSTEM+NT,PFT/CT
L7	20270	SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) CARDIOMYOPATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT OR ISCHEMIA+NT,PFT/CT
L8	9348	SEA FILE=HCAPLUS ABB=ON PLU=ON REPERFUSION+PFT/CT OR "REPERFUSION (L) INJURY"+PFT/CT
L9	335374	SEA FILE=HCAPLUS ABB=ON PLU=ON (L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8)
L14	1	SEA FILE=REGISTRY ABB=ON PLU=ON 186392-65-4/RN
L21	11	SEA FILE=HCAPLUS ABB=ON PLU=ON L14
L28	10	SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND L21
L31	2	SEA FILE=HCAPLUS ABB=ON PLU=ON WO199639384/PN OR WO199639385/PN
L36	9	SEA FILE=HCAPLUS ABB=ON PLU=ON L28 NOT L31

dr's 2, 5th compound

=> FIL REG
FILE 'REGISTRY' ENTERED AT 12:07:15 ON 05 SEP 2002

STRUCTURE FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3
DICTIONARY FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

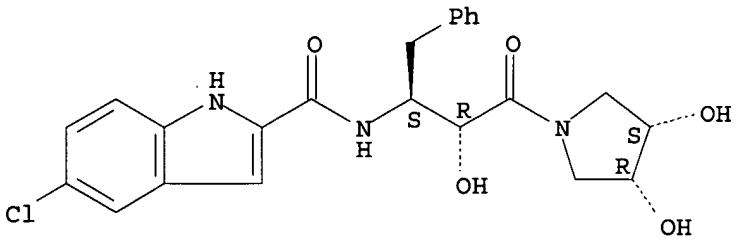
Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> D L14

L14 ANSWER 1 OF 1 REGISTRY

RN **186392-65-4** REGISTRY
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Indole-2-carboxamide, 5-chloro-N-[3-(3,4-dihydroxy-1-pyrrolidinyl)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-, [R-[R*,S*-(cis)]]-
OTHER NAMES:
CN Ingliforib
FS STEREOSEARCH
MF C23 H24 Cl N3 O5
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

11 REFERENCES IN FILE CA (1967 TO DATE)
11 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS
FILE 'HCAPLUS' ENTERED AT 12:07:32 ON 05 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10
FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use

the CAS Roles thesaurus (/RL field) in this file.

=> D IBIB AB HIT L36 1-9

L36 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:936092 HCAPLUS
DOCUMENT NUMBER: 136:53752
TITLE: Synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors
INVENTOR(S): Mylari, Banavara L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 41 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001056095	A1	20011227	US 2001-782798	20010213

PRIORITY APPLN. INFO.: US 2000-183004P P 20000216

AB Mono-, di- and triethanolamine salts of [4-Oxo-(5-trifluoromethylbenzothiazol-2-ylmethyl)-3,4-dihydrophthalazin-1-yl]acetic acid (zopolrestat; I) were prepd. E.g., a soln. of I in acetone was added to ethanolamine (10 mol equiv, room temp., 1 h) which afforded, after purifn., the ethanolamine salt in 95% yield, m.p. 119 - 121.degree.C. Ethanolamine salts of I are used alone or with NHE-1 inhibitors (e.g. II), selective serotonin reuptake inhibitors (SSRIs, e.g. fluoxetine), glycogen phosphorylase inhibitors (GPIs), sorbitol dehydrogenase inhibitors (SDIs) and antihypertensive agents for treating diabetic complications.

IT **Diabetes insipidus**
(complications from)

IT **Heart, disease**
(**diabetic cardiomyopathy**; synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors)

IT **Heart, disease**
(infarction; synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors)

IT **Blood vessel, disease**
(microangiopathy; synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors)

IT 54910-89-3, Fluoxetine 79559-97-0, Sertraline hydrochloride 79617-96-2, Sertraline 106650-56-0, Sibutramine **186392-65-4** 241800-98-6 241801-81-0, [5-Isopropyl-1-(6-quinolinyl)-1H-pyrazole-4-carbonyl]guanidine 241801-83-2, [5-Propyl-1-(6-quinolinyl)-1H-pyrazole-4-carbonyl]guanidine 241801-85-4, [1-(2-Chlorophenyl)-5-methyl-1H-pyrazole-4-carbonyl]guanidine 241801-86-5, [5-Methyl-1-(2-trifluoromethylphenyl)-1H-pyrazole-4-carbonyl]guanidine 241801-87-6, (5-Ethyl-1-phenyl-1H-pyrazole-4-carbonyl)guanidine 241801-88-7, [5-Cyclopropyl-1-(2-trifluoromethylphenyl)-1H-pyrazole-4-carbonyl]guanidine 241801-89-8, (5-Cyclopropyl-1-phenyl-1H-pyrazole-4-carbonyl)guanidine 241801-90-1, [5-Cyclopropyl-1-(2,6-dichlorophenyl)-1H-pyrazole-4-carbonyl]guanidine 241801-93-4, [5-Cyclopropyl-1-(quinolin-8-yl)-1H-pyrazole-4-carbonyl]guanidine 241802-04-0, [1-(2-Chloro-4-methylsulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-05-1, [1-(2-Chlorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine

241802-06-2, [1-(2-Trifluoromethyl-4-fluorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-07-3, [1-(2-Bromophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-08-4, [1-(2-Fluorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-09-5, [1-(2-Chloro-5-methoxyphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-10-8, [1-(2-Chloro-4-methylaminosulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-11-9, [1-(2,5-Dichlorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-12-0, [1-(2,3-Dichlorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-13-1, [1-(2-Chloro-5-aminocarbonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-14-2, [1-(2-Chloro-5-aminosulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-15-3, [1-(2-Fluoro-6-trifluoromethylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-16-4, [1-(2-Chloro-5-methylsulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-17-5, [1-(2-Chloro-5-dimethylaminosulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-18-6, [1-(2-Trifluoromethyl-4-chlorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-19-7, [1-(8-Bromoquinolin-5-yl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-20-0, [1-(6-Chloroquinolin-5-yl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-21-1, [1-(Indazol-7-yl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-22-2, [1-(Benzimidazol-5-yl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-23-3, [1-(1-Isoquinolyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-24-4, [5-Cyclopropyl-1-(4-quinolinyl)-1H-pyrazole-4-carbonyl]guanidine 241802-25-5, [1-(Indazol-6-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-26-6, [1-(Indazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-27-7, [1-(Benzimidazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-28-8, [1-(1-Methylbenzimidazol-6-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-29-9, [1-(5-Quinolinyl)-5-n-propyl-1H-pyrazole-4-carbonyl]guanidine 241802-30-2, [1-(5-Quinolinyl)-5-isopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-31-3, [5-Ethyl-1-(6-quinolinyl)-1H-pyrazole-4-carbonyl]guanidine 241802-32-4, [1-(2-Methylbenzimidazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-33-5, [1-(1,4-Benzodioxan-6-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-34-6, [1-(Benzotriazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-35-7, [1-(3-Chloroindazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-36-8, [1-(5-Quinolinyl)-5-butyl-1H-pyrazole-4-carbonyl]guanidine 300548-76-9, 1(R)-[4-[1'-[2-(1(R)-Hydroxyethyl)pyrimidin-4-yl]-[4,4']bipiperidinyl-1-yl]pyrimidin-2-yl]ethanol 300548-89-4 300548-90-7 300548-92-9, 1R-[4-[4-(2-Hydroxymethyl-6-methylpyrimidin-4-yl)-3S-methylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300548-93-0 300548-99-6 300549-00-2, 1R-[4-[4-(4,6-Dimethylpyrimidin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300549-02-4, 1R-[4-[4-(4-Hydroxymethyl-6-methylpyrimidin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300549-03-5, 1R-[4-[4-(2,6-Dimethylpyrimidin-4-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300549-05-7, 1R-[4-[4-(2-Hydroxymethyl-6-methylpyrimidin-4-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300549-16-0, 1R-[4-[4-(2-Hydroxymethylpyrimidin-4-yl)-3S-methylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300549-28-4 300549-30-8 300549-32-0 300549-34-2 300549-50-2 300549-51-3 300549-53-5 300549-58-0, 1R-[4-[4-(4-Hydroxymethyl-6-methylpyrimidin-2-yl)-3S-methylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300550-38-3 300550-60-1 300550-69-0 300551-01-3, 1R-[4-[2R,6S-Dimethyl-4-[2-(4-methylimidazol-1-yl)pyrimidin-4-yl]piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-03-5, 1R-[4-[4-[2-(2,4-Dimethylimidazol-1-yl)pyrimidin-4-yl]-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-04-6 300551-11-5,

1R-[4-[2R,6S-Dimethyl-4-[2-(4-methylpiperazin-1-yl)pyrimidin-4-yl]piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-12-6, 1R-[4-[2R,6S-Dimethyl-4-(2-morpholin-4-ylpyrimidin-4-yl)piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-17-1, 1R-[4-[3R,5S-Dimethyl-4-[2-(4-methylpiperazin-1-yl)pyrimidin-4-yl]piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-19-3, 1R-[4-[4-[2-(4-Ethylpiperazin-1-yl)pyrimidin-4-yl]-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-20-6, 1R-[4-[4-[2-(4-Isopropylpiperazin-1-yl)pyrimidin-4-yl]-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-21-7, 1R-[4-[2R,6S-Dimethyl-4-(4-morpholin-4-yl-[1,3,5]triazin-2-yl)piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-22-8, 1R-[4-[4-(4-Methoxy-6-methyl-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-23-9, 1R-[4-[4-(4,6-Dimethoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-24-0, 1R-[4-[2R,6S-Dimethyl-4-(4-phenyl-[1,3,5]triazin-2-yl)piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-28-4, 1R-[4-[3R,5S-Dimethyl-4-[4-methyl-6-(4-methylpiperazin-1-yl)-[1,3,5]triazin-2-yl]piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-29-5, 1R-[4-[2R,6S-Dimethyl-4-(4-methyl-[1,3,5]triazin-2-yl)piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-30-8, 1R-[4-[4-(4,6-Dimethoxy-[1,3,5]triazin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-31-9, 1R-[4-[4-(4-Ethoxy-6-methyl-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-32-0, 1R-[4-[4-(4-Isopropoxy-6-methyl-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-33-1, 1R-[4-[3R,5S-Dimethyl-4-(4-phenyl-[1,3,5]triazin-2-yl)piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-42-2, 1R-[4-[4-(4-Cyclopropyl-[1,3,5]triazin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-43-3 300551-45-5, 1R-[4-[4-(4-Hydroxymethyl-6-methoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-48-8, 1R-[4-[4-(4-Hydroxymethyl-6-phenyl-[1,3,5]triazin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-49-9, 1R-[4-[4-(4,6-Dimethyl-[1,3,5]triazin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-50-2, 1R-[4-[4-(4,6-Dimethyl-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-52-4, 1R-[4-[3R,5S-Dimethyl-4-(4-methyl-6-phenyl-[1,3,5]triazin-2-yl)piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-87-5 300551-88-6 300551-89-7 300551-90-0 300551-91-1 300551-92-2 300551-94-4 300551-95-5 300551-96-6, 1R-[4-[3R,5S-Dimethyl-4-[2-(4-methylimidazol-1-yl)pyrimidin-4-yl]piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-97-7, 1R-[4-[3R,5S-Dimethyl-4-[2-(2-methylimidazol-1-yl)pyrimidin-4-yl]piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-98-8, 1R-[4-[4-[2-(2,4-Dimethylimidazol-1-yl)pyrimidin-4-yl]-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-99-9, 1R-[4-[4-(4-Isopropoxy-6-methoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300552-00-5, 1R-[4-[4-(4-Isopropyl-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300552-02-7, 1R-[4-[4-(4-Ethyl-6-methoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300552-03-8, 1R-[4-[4-[2-(4-Ethylpiperazin-1-yl)pyrimidin-4-yl]-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300552-04-9, 1R-[4-[4-(4-Methoxy-6-methoxymethyl-[1,3,5]triazin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300552-06-1, 1R-[4-[4-(4-Methoxy-6-methyl-[1,3,5]triazin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300552-07-2 382142-96-3 382143-00-2 382143-43-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination pharmaceutical; synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors)

L36 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:709687 HCAPLUS
DOCUMENT NUMBER: 135:272869
TITLE: Synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136071	A2	20010926	EP 2001-301979	20010305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001302546	A2	20011031	JP 2001-78839	20010319

PRIORITY APPLN. INFO.: US 2000-191381P P 20000322
OTHER SOURCE(S): MARPAT 135:272869

AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH2, CH-alkyl when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6- or 7-NO2, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R2 = H; R3 = H, alkyl; R4 = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R5 = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R7 = H, F, alkyl; or R5 and R7 can be taken together to be oxo; R6 = carboxy, alkoxycarbonyl, amido, acyl, alkyl, OH, alkoxy; R9 = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and derivs. were prepd. Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydroxypyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF, HOBt, EDC, room temp.) to give amide II. Compds. I are glycogen phosphorylase inhibitors used for treating type 2 diabetes mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-glycogen phosphorylase inhibiting anti-diabetic agents are also claimed.

IT **Diabetes mellitus**
(non-insulin-dependent; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

IT 186392-40-5P 186392-46-1P 186392-47-2P 186392-49-4P 186392-51-8P
186392-52-9P 186392-53-0P 186392-64-3P **186392-65-4P**
186392-70-1P 186429-64-1P 186429-91-4P 186430-03-5P 186430-23-9P
186430-41-1P 186430-83-1P 186431-27-6P 186431-28-7P 186431-29-8P
225929-30-6P 251446-20-5P 251446-21-6P 251446-22-7P 251446-23-8P
251446-24-9P 251446-25-0P 251446-26-1P 251446-27-2P 251446-28-3P
251446-29-4P 251446-30-7P 251446-31-8P 251446-32-9P 251446-33-0P
251446-34-1P 251446-35-2P 332098-11-0P 332098-12-1P 332098-13-2P
332098-14-3P 332098-15-4P 332098-16-5P 332098-17-6P 332098-18-7P
332098-19-8P 332098-20-1P 332098-21-2P 332098-22-3P 332098-23-4P
332098-24-5P 332098-25-6P 332098-26-7P 332098-27-8P 332098-28-9P
332098-29-0P 332098-30-3P 332098-31-4P 332098-32-5P 332098-33-6P
332098-34-7P 332098-35-8P 332098-36-9P 332098-37-0P 332098-38-1P
332098-39-2P 332098-40-5P 332098-41-6P 332098-42-7P 332098-43-8P
332098-44-9P 332098-45-0P 332098-46-1P 332098-47-2P 332098-48-3P
332098-49-4P 332098-50-7P 332098-52-9P 332098-54-1P 332098-55-2P
332098-57-4P 332098-59-6P 332098-61-0P 332098-63-2P 332098-65-4P
362521-64-0P 362521-65-1P 362521-66-2P 362521-89-9P 362521-91-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

L36 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:693088 HCAPLUS
DOCUMENT NUMBER: 135:262225
TITLE: Glycogen phosphorylase inhibitor compositions
INVENTOR(S): Babcock, Walter C.; Friesen, Dwayne Thomas; Lorenz, Douglas Alan; Macri, Christopher A.; Nightingale, James Alan Schriver; Shanker, Ravi Mysore; Hancock, Bruno Caspar; Crew, Marshall D.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068092	A2	20010920	WO 2001-IB389	20010316
WO 2001068092	A3	20020321		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001053791	A1	20011220	US 2001-808559	20010314

PRIORITY APPLN. INFO.: US 2000-190125P P 20000316

AB Pharmaceutical compns. of a particularly effective sparingly sol. glycogen phosphorylase inhibitor are disclosed. Thus, an amorphous solid dispersion contg. 25% a drug and 75% polymer was made by first mixing the drug in acetone together with a finely powd. HPMCAS to form a soln. The soln. comprised 1.25% drug, 3.75% HPMCAS, and 95% acetone. This soln. was then spray-dried by directing an atomizing spray via a 2-fluid external mix spray nozzle at 2.6 bar at a 175 to 180 g/min feed rate into a stainless steel chamber of a NIRO XP spray drier, maintained at a temp. of 180.degree. at the inlet and 69.degree. at the outlet.

IT **186392-65-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(glycogen phosphorylase inhibitor compns.)

IT **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitor**; glycogen phosphorylase **inhibitor** compns.)

IT **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitor**; glycogen phosphorylase **inhibitor** compns.)

L36 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:693054 HCAPLUS
DOCUMENT NUMBER: 135:247221
TITLE: Pharmaceutical compositions containing glycogen phosphorylase inhibitors
INVENTOR(S): Hoover, Dennis Jay; Shanker, Ravi Mysore; Friesen, Dwayne Thomas; Lorenz, Douglas Alan; Nightingale, James Alan Schriver
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068055	A1	20010920	WO 2001-IB394	20010316
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001053778	A1	20011220	US 2001-805828	20010314

PRIORITY APPLN. INFO.: US 2000-189942P P 20000316
OTHER SOURCE(S): MARPAT 135:247221

AB Pharmaceutical compns. comprise a glycogen phosphorylase inhibitor and at least one concn.-enhancing polymer. The compn. may be a simple phys. mixt. of glycogen phosphorylase inhibitor and concn.-enhancing polymer or a dispersion of glycogen phosphorylase inhibitor and polymer. A dispersion of 25% 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3R,4S)-dihydroxypyrrolidin-1-yl)-3-oxypropyl]amide and 75% polymer was made by first mixing the drug in acetone together with HPMCAS to form a soln. The soln. comprised 1.25 drug, 3.75% HPMCAS, and 95% acetone. This soln. was then spray-dried by directing an atomizing spray using a 2-fluid external-mix spray nozzle at 2.6 bar at a feed rate of 175 to 180 g/min into the stainless-steel chamber of a spray-dryer, maintained at 180.degree. on the inlet and 69.degree. at the outlet. The resulting amorphous solid spray-dried dispersion was collected and then dried in a solvent tray-dryer by spreading the spray-dried particles onto polyethylene-lined trays to a depth of not >1 cm and then drying them at 40.degree. for at least 8 h.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Heart, disease**
(**diabetic cardiomyopathy**; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)
IT **Heart, disease**
(**ischemia**; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)
IT **Diabetes mellitus**
(non-insulin-dependent; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)
IT Antitumor agents
Atherosclerosis
Cataract

Digestive tract
Dissolution rate
Drug bioavailability
Hypercholesterolemia
Hyperglycemia
Hypertension
Hypertriglyceridemia
Ischemia
Solubility
Solvent effect
(pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**inhibitors**; pharmaceutical compns. contg. glycogen phosphorylase **inhibitors**)

IT 186392-40-5 186392-43-8 186392-51-8 186392-53-0 186392-63-2
186392-65-4 186429-91-4 186430-03-5 186430-23-9
186430-40-0 186430-57-9 186431-27-6 251446-20-5 251446-21-6
251446-32-9 332098-16-5 332098-17-6 361176-31-0
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

L36 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:554794 HCAPLUS
DOCUMENT NUMBER: 135:132447
TITLE: Chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123

PRIORITY APPLN. INFO.: US 2000-177770P P 20000124

AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylmethyl)-2-phenylethyl]amide, etc., and their prodrugs are claimed as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy. The title compds. can also combine with insulin, insulin analogs (biguanides), .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma. agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors, .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid receptor antagonists, and/or thyroid hormone analogs for treatment of diabetes, cardiovascular diseases, heart ischemia, congestive heart failure, hypertension, diabetic angiopathy, myocardial infarction, etc.

IT **Blood vessel, disease**
(diabetic angiopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(**diabetic cardiomyopathy**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Cardiovascular system**
(disease; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(failure; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**
(infarction; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**
(**ischemia**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT 56-03-1D, Biguanide, derivs. 504-75-6D, Imidazoline, derivs. 7440-62-2D, Vanadium, salts, biological studies 9004-10-8, Insulin, biological studies 97322-87-7D, TroGlitazone, derivs. 186392-21-2 186392-39-2 186392-40-5 186392-49-4 **186392-65-4** 186392-67-6 186392-70-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase **inhibitors** for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

L36 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:489208 HCAPLUS
DOCUMENT NUMBER: 135:97443
TITLE: Pharmaceutical compositions containing polymer for enhanced drug concentrations
INVENTOR(S): Babcock, Walter Christian; Curatolo, William John; Friesen, Dwayne Thomas; Lorenz, Douglas Alan; Nightingale, James Alan Schriver; Shanker, Ravi Mysore
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047495	A1	20010705	WO 2000-IB1787	20001201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002006443	A1	20020117	US 2000-742785	20001220

PRIORITY APPLN. INFO.: US 1999-171841P P 19991223

AB A drug in a soly.-improved form is combined with a concn.-enhancing polymer, i.e., a cellulosic or non-cellulosic polymer, in a sufficient amt. so that the combination provides substantially enhanced drug concn. in a use environment,, such as digestive tract, s.c. space, vagina, lung, blood vessels, and muscle relative to a control comprising the same amt. of the same soly.-improved form of drug without the concn.-enhancing polymer. For example, the soly. of sertraline-HCl was increased in presence of citric acid, giving a soly.-improvement factor of 9.3. Thus, citric acid is an excellent solubilizing agent for sertraline-HCl. A soln. was prepd. contg. 1000 .mu.g/mL sertraline-HCl, 500 .mu.g/mL citric acid, and 1000 .mu.g/mL hydroxypropyl Me cellulose acetate succinate (HPMCAS) in phosphate buffer. (pH 7.9). Addn. of the concn.-enhancing polymer HPMCAS resulted in a max. concn. that was 1.7-fold that of control contg. no polymer.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Artery**
Crystallization
Digestive tract
Dissolution rate
Drug delivery systems
Lung
Muscle
Polyelectrolytes
Solubility
Solubilization
Solubilizers
Vagina
Vein
(pharmaceutical compns. contg. polymer for enhanced drug concns.)

IT 9004-38-0, Cellulose acetate phthalate 9004-58-4, Hydroxyethyl ethyl cellulose 9004-63-1, Hydroxyethyl cellulose acetate 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5, Methyl cellulose 9032-42-2, Hydroxyethyl methyl cellulose 9050-31-1, Hydroxypropyl methyl cellulose phthalate 52907-01-4, Cellulose acetate trimellitate 54391-89-8, Cellulose acetate terephthalate 58858-21-2, Hydroxypropyl methyl cellulose acetate 67165-96-2, Hydroxypropyl methyl cellulose acetate phthalate 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate 79559-97-0, Sertraline hydrochloride 89233-51-2, Cellulose propionate phthalate 167077-74-9, Cellulose propionate trimellitate 167077-75-0, Cellulose butyrate trimellitate 185021-64-1, Ziprasidone mesylate **186392-65-4** 188979-58-0 219736-80-8 248594-19-6 249296-43-3 288141-80-0, Methyl cellulose acetate phthalate 288156-14-9, Hydroxypropyl methyl cellulose acetate trimellitate 288307-50-6, Hydroxypropyl cellulose butyrate phthalate 288307-51-7, Cellulose acetate isophthalate

288372-69-0, Ethyl phthalic acid cellulose acetate 288372-70-3, Hydroxypropyl cellulose acetate phthalate succinate 288372-71-4, Methyl cellulose acetate trimellitate 288372-72-5, Ethyl cellulose acetate trimellitate 288372-73-6, Hydroxypropyl cellulose acetate trimellitate 288372-74-7, Hydroxypropyl cellulose acetate trimellitate succinate 288372-75-8, Cellulose acetate pyridinedicarboxylate 288372-76-9 288372-77-0 288372-80-5, Ethyl nicotinic acid cellulose acetate 288372-81-6, Ethyl picolinic acid cellulose acetate 348078-72-8 348078-73-9
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmaceutical compns. contg. polymer for enhanced drug concns.)

L36 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:573515 HCAPLUS
DOCUMENT NUMBER: 133:182970
TITLE: Matrix controlled release device for a low-solubility drug
INVENTOR(S): Appel, Leah Elizabeth; Friesen, Dwayne Thomas; Curatolo, William John; Nightingale, James Alan Schriver; Thombre, Avinash Govind
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1027887	A2	20000816	EP 2000-300546	20000126
EP 1027887	A3	20010228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000229888	A2	20000822	JP 2000-33446	20000210
BR 2000000359	A	20010814	BR 2000-359	20000210

PRIORITY APPLN. INFO.: US 1999-119400P P 19990210

AB Disclosed are a controlled release dosage form for a low soly. drug that is a spray-dried or spray-coated amorphous solid dispersion of the drug in an ionizable cellulosic polymer matrix that is in turn incorporated into a secondary erodible polymeric matrix and a method of treating a disease or disorder comprising administering such a dosage form. A batch of solid dispersion was prepd. by spray-drying a soln. contg. drug 5-chloro-1H-indole-2-carboxylic acid [(1S-benzyl-3-(3R,4S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-3-oxypropyl]amide (water soly. 80 .mu.g/mL) in acetone together with hydroxypropyl Me cellulose acetate succinate. The resulting solid dispersion was mixed with hydroxypropyl Me cellulose, lactose, and Mg stearate. The mixt. was finally compressed to give tablets.

IT 67-52-7D, 2,4,6(1H,3H,5H)-Pyrimidinetrione, derivs. 9003-01-4, Polyacrylic acid 9004-38-0, Cellulose acetate phthalate 9004-62-0, Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5, Methyl cellulose 9032-42-2, Hydroxyethyl methyl cellulose 9032-50-2, Methyl cellulose phthalate 19216-56-9, Prazosin 21829-25-4, Nifedipine 25086-15-1, Methacrylic acid-methyl methacrylate copolymer 25087-26-7, Polymethacrylic acid 25300-64-5, Styrene-maleic acid copolymer 25609-89-6, Crotonic acid-vinyl acetate copolymer 29094-61-9, Glipizide 35795-16-5, Trimazosin 37324-30-4, Hydroxypropyl cellulose phthalate 52907-01-4,

Cellulose acetate trimellitate 53237-50-6 54391-89-8, Cellulose acetate terephthalate 54910-89-3, Fluoxetine 56509-23-0, Sodium cellulose acetate phthalate 67165-96-2, Hydroxypropyl methyl cellulose acetate phthalate 68130-20-1, Starch phthalate 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate 74191-85-8, Doxazosin 76974-66-8, Hydroxypropyl cellulose acetate succinate 79617-96-2, Sertraline 88527-84-8, Amylose acetate phthalate 89233-51-2, Cellulose propionate phthalate 93413-69-5, Venlafaxine 96299-43-3, Styrene-maleic acid-dibutyl phthalate copolymer 96352-13-5, Hydroxypropyl ethyl cellulose phthalate 139755-83-2, Sildenafil 146939-27-7, Ziprasidone 167077-74-9 167077-75-0, Cellulose butyrate trimellitate **186392-65-4** 188979-58-0 252856-84-1, Poly(vinyl acetate hydrogen phthalate) 288141-80-0, Methyl cellulose acetate phthalate 288154-33-6 288156-14-9 288297-68-7 288297-69-8 288307-47-1, Hydroxyethyl methyl cellulose acetate phthalate 288307-48-2, Hydroxyethyl methyl cellulose acetate succinate 288307-50-6, Hydroxypropyl cellulose butyrate phthalate 288307-51-7, Cellulose acetate isophthalate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cellulosic polymer and pH-sensitive polymer matrixes for solid dispersion of low-soly. drugs)

IT 9001-03-0, Carbonic anhydrase **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; cellulosic polymer and pH-sensitive polymer matrixes for solid dispersion of low-soly. drugs)

L36 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:566034 HCAPLUS
DOCUMENT NUMBER: 131:199699
TITLE: N-[(Substituted five-membered di- or triaza diunsaturated ring)carbonyl]guanidine derivatives for the treatment of ischemia
INVENTOR(S): Hamanaka, Ernest S.; Guzman-Perez, Angel; Ruggeri, Roger B.; Wester, Ronald T.; Mularski, Christian J.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 246 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943663	A1	19990902	WO 1999-IB206	19990205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2321642	AA	19990902	CA 1999-2321642	19990205
AU 9920706	A1	19990915	AU 1999-20706	19990205
AU 739403	B2	20011011		
BR 9908332	A	20001107	BR 1999-8332	19990205
EP 1056729	A1	20001206	EP 1999-901083	19990205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,				

SI, LT, LV, FI, RO

JP 2002504546	T2	20020212	JP 2000-533420		19990205
ZA 9901578	A	20000828	ZA 1999-1578		19990226
NO 2000004192	A	20000822	NO 2000-4192		20000822
PRIORITY APPLN. INFO.:			US 1998-76362P	P	19980227
			WO 1999-IB206	W	19990205

OTHER SOURCE(S): MARPAT 131:199699

AB Guanidine derivs. ZCON:C(NH2)2 [I; Z = certain (un)substituted, diunsatd., diazoles and triazoles] and their pharmaceutically acceptable salts and/or prodrugs are disclosed, for use as inhibitors of sodium-hydrogen exchanger type 1 (NHE-1). Also disclosed are methods of using I, and pharmaceutical compns. contg. them. I are useful for the redn. of tissue damage resulting from tissue ischemia (no data). A large no. of compds. I and their intermediates were prepd. and/or specifically claimed. For instance, guanidine-HCl was converted to the free base, taken up in THF-DMF mixt., and coupled with 5-methyl-2-(2-methoxyphenyl)-2H-1,2,3-triazole-4-carboxylic acid (pre-activated with carbonyldiimidazole), and the resultant guanidine deriv. was isolated and acidified with HCl in MeOH, to give title compd. II.HCl in 17% yield.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Brain, disease
Heart, disease
Intestine, disease
Kidney, disease
Liver, disease
Lung, disease
Muscle, disease
Pancreas, disease
Spleen
(**ischemia**; prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of **ischemia**)

IT **Ischemia**
(prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of ischemia)

IT 9028-31-3, Aldose reductase **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(pharmaceuticals also contg. **inhibitors** of; prepn. of diazole and triazole guanidine derivs. as NHE-1 **inhibitors** for treatment of ischemia)

IT 110703-94-1, 3,4-Dihydro-4-oxo-3-[[5-(trifluoromethyl)-2-benzothiazolyl]methyl]-1-phthalazineacetic acid 186392-40-5
186392-43-8 186392-49-4 186392-53-0 186392-64-3 **186392-65-4**
186429-64-1 186429-78-7 186429-91-4 186430-03-5 186430-23-9
186430-41-1 186430-57-9 186431-27-6 225929-30-6
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceuticals contg.; prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of ischemia)

L36 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:193899 HCAPLUS
DOCUMENT NUMBER: 130:227741
TITLE: Solid pharmaceutical dispersions with enhanced bioavailability
INVENTOR(S): Curatolo, William John; Herbig, Scott Max; Nightingale, James Alan Schriver
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 46 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 901786	A2	19990317	EP 1998-305960	19980727
EP 901786	A3	20000119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1207896	A	19990217	CN 1998-116282	19980810
JP 11116502	A2	19990427	JP 1998-227328	19980811
JP 2984661	B2	19991129		
BR 9803144	A	20000111	BR 1998-3144	19980811
US 2002009494	A1	20020124	US 2001-770562	20010126
PRIORITY APPLN. INFO.:			US 1997-55221P P	19970811
			US 1998-131019 B1	19980807

AB Spray dried solid dispersions comprising a sparingly sol. drug and hydroxypropyl Me cellulose acetate succinate (HPMCAS) provide increased aq. soly. and/or bioavailability in a use environment. Spray dried compns. were prepd. from HPMCAS and compds. such as ziprasidone, griseofulvin, nifedipine and phenytoin.

IT 9015-71-8, Corticotropin releasing hormone **9035-74-9**, Glycogen phosphorylase 80619-02-9, 5-Lipoxygenase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; solid pharmaceutical dispersions with enhanced bioavailability)

IT 57-41-0, Phenytoin 126-07-8, Griseofulvin 21829-25-4, Nifedipine 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate 146939-27-7, Ziprasidone 175139-41-0 175140-00-8 186392-43-8 **186392-65-4** 221163-46-8
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(solid pharmaceutical dispersions with enhanced bioavailability)

=> FIL STNGUIDE
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Aug 30, 2002 (20020830/UP).

=> D QUE L37
L1 6031 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHORYLASE+PFT/CT OR PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI
L2 465 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 (L) (INHIBIT? OR ANTAGONI?)
L3 153 SEA FILE=HCAPLUS ABB=ON PLU=ON (ANTIDIABETIC AGENTS+NT,PFT/CT OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR PKT OR DMA)/RL
L4 47128 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABETES INSIPIDUS+NT,PFT/CT OR DIABETES MELLITUS+NT,PFT/CT
L5 304 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) DIABETIC CARDIOMYOPATHY"+PFT/CT
L6 287453 SEA FILE=HCAPLUS ABB=ON PLU=ON CARDIOVASCULAR SYSTEM+NT,PFT/CT

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L7        20270 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HEART, DISEASE (L) CARDIOMYOP
                ATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT
                OR ISCHEMIA+NT,PFT/CT
L8         9348 SEA FILE=HCAPLUS ABB=ON  PLU=ON  REPERFUSION+PFT/CT OR
                "REPERFUSION (L) INJURY"+PFT/CT
L9       335374 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L2 OR L3 OR L4 OR L5 OR L6
                OR L7 OR L8)
L15           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  186392-67-6/RN  claim 2, 6th compound
L22           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15
L29           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L22
L31           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  WO199639384/PN OR WO199639385/
                PN
L37           1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 NOT L31


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STRUCTURE FILE UPDATES:    4 SEP 2002  HIGHEST RN 446821-48-3
DICTIONARY FILE UPDATES:   4 SEP 2002  HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Calculated physical property data is now available.  See HELP PROPERTIES
for more information.  See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> D L15

L15  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2002 ACS
RN   186392-67-6  REGISTRY
CN   1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methyl-2-
     pyridinylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1H-Indole-2-carboxamide, 5-chloro-N-[2-hydroxy-3-(methyl-2-pyridinylamino)-
     3-oxo-1-(phenylmethyl)propyl]-, [R-(R*,S*)]-
FS   STEREOSEARCH
MF   C25 H23 Cl N4 O3
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
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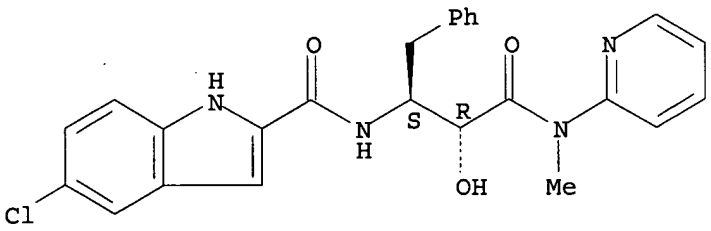

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS
FILE 'HCAPLUS' ENTERED AT 12:09:22 ON 05 SEP 2002
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FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10
FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> D IBIB AB HIT L37

L37 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:554794 HCAPLUS
DOCUMENT NUMBER: 135:132447
TITLE: Chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123

PRIORITY APPLN. INFO.: US 2000-177770P P 20000124

AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylmethyl)-2-phenylethyl]amide, etc., and their prodrugs are claimed as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy. The title compds. can also combine with insulin, insulin analogs (biguanides), .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma. agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors, .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid receptor antagonists, and/or thyroid hormone analogs for treatment of diabetes, cardiovascular diseases, heart ischemia, congestive heart failure, hypertension, diabetic angiopathy, myocardial infarction, etc.

IT **Blood vessel, disease**
(diabetic angiopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(**diabetic cardiomyopathy**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Cardiovascular system**
(disease; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(failure; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**
(infarction; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**
(**ischemia**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT 56-03-1D, Biguanide, derivs. 504-75-6D, Imidazoline, derivs. 7440-62-2D, Vanadium, salts, biological studies 9004-10-8, Insulin, biological studies 97322-87-7D, TroGlitazone, derivs. 186392-21-2 186392-39-2 186392-40-5 186392-49-4 186392-65-4 **186392-67-6** 186392-70-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and

other cardiovascular diseases)
IT **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase **inhibitors** for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

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=> FIL STNGUIDE
FILE 'STNGUIDE' ENTERED AT 12:09:38 ON 05 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Aug 30, 2002 (20020830/UP).

=> D QUE L38
L1          6031 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHORYLASE+PFT/CT OR
                 PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI
L2           465 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1 (L) (INHIBIT? OR ANTAGONI?)

L3           153 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (ANTIDIABETIC AGENTS+NT,PFT/CT
                  OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR
                 PKT OR DMA)/RL
L4         47128 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DIABETES INSIPIDUS+NT,PFT/CT
                 OR DIABETES MELLITUS+NT,PFT/CT
L5           304 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HEART, DISEASE (L) DIABETIC
                 CARDIOMYOPATHY"+PFT/CT
L6         287453 SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARDIOVASCULAR SYSTEM+NT,PFT/C
                 T
L7          20270 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HEART, DISEASE (L) CARDIOMYOP
                 ATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT
                 OR ISCHEMIA+NT,PFT/CT
L8           9348 SEA FILE=HCAPLUS ABB=ON  PLU=ON  REPERFUSION+PFT/CT OR
                 "REPERFUSION (L) INJURY"+PFT/CT
L9         335374 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L2 OR L3 OR L4 OR L5 OR L6
                 OR L7 OR L8)
L16             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  186392-70-1/RN
L23             4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16
L30             3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 AND L23
L31             2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  WO199639384/PN OR WO199639385/
                 PN
L38             2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30 NOT L31
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7th compound, claim 2

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=> FIL REG
FILE 'REGISTRY' ENTERED AT 12:10:22 ON 05 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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STRUCTURE FILE UPDATES:    4 SEP 2002  HIGHEST RN 446821-48-3
DICTIONARY FILE UPDATES:   4 SEP 2002  HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.
```

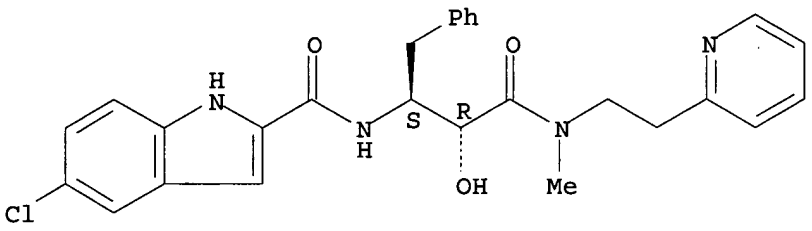
Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> D L16

L16 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN **186392-70-1** REGISTRY
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[methyl[2-(2-pyridinyl)ethyl]amino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-hydroxy-3-[methyl[2-(2-pyridinyl)ethyl]amino]-3-oxo-1-(phenylmethyl)propyl]-, [R-(R*,S*)]-
FS STEREOSEARCH
MF C27 H27 Cl N4 O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS
FILE 'HCAPLUS' ENTERED AT 12:10:35 ON 05 SEP 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10

FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> D IBIB AB HIT L38 1-2

L38 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:709687 HCAPLUS
DOCUMENT NUMBER: 135:272869
TITLE: Synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136071	A2	20010926	EP 2001-301979	20010305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001302546	A2	20011031	JP 2001-78839	20010319

PRIORITY APPLN. INFO.: US 2000-191381P P 20000322
OTHER SOURCE(S): MARPAT 135:272869

AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH2, CH-alkyl when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6- or 7-NO2, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R2 = H; R3 = H, alkyl; R4 = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R5 = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R7 = H, F, alkyl; or R5 and R7 can be taken together to be oxo; R6 = carboxy, alkoxycarbonyl, amido, acyl, alkyl, OH, alkoxy; R9 = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and derivs. were prepd. Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydroxypyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF, HOBt, EDC, room temp.) to give amide II. Compds. I are glycogen phosphorylase inhibitors used for treating type 2 diabetes mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-glycogen phosphorylase inhibiting anti-diabetic agents are also claimed.

IT **Diabetes mellitus**
(non-insulin-dependent; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

IT 186392-40-5P 186392-46-1P 186392-47-2P 186392-49-4P 186392-51-8P
186392-52-9P 186392-53-0P 186392-64-3P 186392-65-4P
186392-70-1P 186429-64-1P 186429-91-4P 186430-03-5P
186430-23-9P 186430-41-1P 186430-83-1P 186431-27-6P 186431-28-7P
186431-29-8P 225929-30-6P 251446-20-5P 251446-21-6P 251446-22-7P
251446-23-8P 251446-24-9P 251446-25-0P 251446-26-1P 251446-27-2P

251446-28-3P 251446-29-4P 251446-30-7P 251446-31-8P 251446-32-9P
251446-33-0P 251446-34-1P 251446-35-2P 332098-11-0P 332098-12-1P
332098-13-2P 332098-14-3P 332098-15-4P 332098-16-5P 332098-17-6P
332098-18-7P 332098-19-8P 332098-20-1P 332098-21-2P 332098-22-3P
332098-23-4P 332098-24-5P 332098-25-6P 332098-26-7P 332098-27-8P
332098-28-9P 332098-29-0P 332098-30-3P 332098-31-4P 332098-32-5P
332098-33-6P 332098-34-7P 332098-35-8P 332098-36-9P 332098-37-0P
332098-38-1P 332098-39-2P 332098-40-5P 332098-41-6P 332098-42-7P
332098-43-8P 332098-44-9P 332098-45-0P 332098-46-1P 332098-47-2P
332098-48-3P 332098-49-4P 332098-50-7P 332098-52-9P 332098-54-1P
332098-55-2P 332098-57-4P 332098-59-6P 332098-61-0P 332098-63-2P
332098-65-4P 362521-64-0P 362521-65-1P 362521-66-2P 362521-89-9P
362521-91-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

IT **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(synthesis of indolyl-amides as glycogen phosphorylase **inhibitors** for treatment of type 2 diabetes)

L38 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:554794 HCAPLUS
DOCUMENT NUMBER: 135:132447
TITLE: Chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123

PRIORITY APPLN. INFO.: US 2000-177770P P 20000124
AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylmethyl)-2-phenylethyl]amide, etc., and their prodrugs are claimed as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy. The title compds. can also combine with insulin, insulin analogs (biguanides), .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma. agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors, .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid receptor antagonists, and/or thyroid hormone analogs for treatment of diabetes, cardiovascular diseases, heart ischemia, congestive heart failure, hypertension, diabetic angiopathy, myocardial infarction, etc.

IT **Blood vessel, disease**
(diabetic angiopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(**diabetic cardiomyopathy**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Cardiovascular system**
(disease; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**
(failure; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**
(infarction; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**
(**ischemia**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT 56-03-1D, Biguanide, derivs. 504-75-6D, Imidazoline, derivs. 7440-62-2D, Vanadium, salts, biological studies 9004-10-8, Insulin, biological studies 97322-87-7D, TroGlitazone, derivs. 186392-21-2 186392-39-2 186392-40-5 186392-49-4 186392-65-4 186392-67-6 **186392-70-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase **inhibitors** for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

Generic Structure Search

display query for line 31 (L31)

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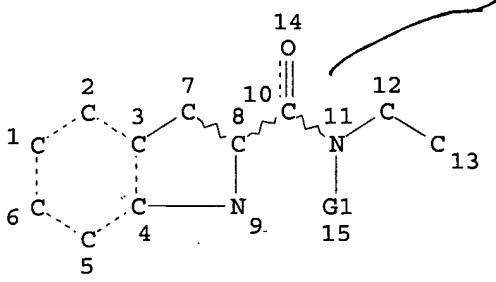

undefined bonds to allow for resonance structures and/or tautomer structures.

Point of Contact:
Thomas G. Larson, Ph.D.
703-308-7309
CM1, Rm. 6 B 01

VAR G1=H/16 = R_3 = H or Alkyl-(see node 16 above).
NODE ATTRIBUTES:
CONNECT IS E2 RC AT 9
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS M1-X5 C AT 16 — size of alkyl group @ node 16 is limited to minimum of 1 to maximum of 5 (m1-x5) carbons.

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

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L3  (       473) SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2
L4  (         1) SEA FILE=REGISTRY ABB=ON  PLU=ON  9035-74-9/RN
L5  (      4127) SEA FILE=HCAPLUS ABB=ON  PLU=ON  L4
L6  (      6031) SEA FILE=HCAPLUS ABB=ON  PLU=ON  PHOSPHORYLASE+PFT/CT OR
                 PHOSPHORYLASE B+PFT/CT OR L5
L7  (       465) SEA FILE=HCAPLUS ABB=ON  PLU=ON  L6 (L) (INHIBIT? OR ANTAGONI?)

L8  (        16) SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7 AND L3
L9  (     10520) SEA FILE=HCAPLUS ABB=ON  PLU=ON  ANTIDIABETIC AGENTS+NT,PFT/CT

L10 (        26) SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L9
L11 (     47097) SEA FILE=HCAPLUS ABB=ON  PLU=ON  DIABETES INSIPIDUS+NT,PFT/CT
                 OR DIABETES MELLITUS+NT,PFT/CT
L12 (        14) SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L11
L13 (       304) SEA FILE=HCAPLUS ABB=ON  PLU=ON  "HEART, DISEASE (L) DIABETIC
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L14 (         3) SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L13
L15 (     57969) SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARDIOVASCULAR AGENTS+NT,PFT/C
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L19 (    287361) SEA FILE=HCAPLUS ABB=ON  PLU=ON  CARDIOVASCULAR SYSTEM+NT,PFT/C
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                 PFT/CT
L22 (        13) SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L21
L23 (      9343) SEA FILE=HCAPLUS ABB=ON  PLU=ON  REPERFUSION+PFT/CT OR
                 "REPERFUSION (L) INJURY"+PFT/CT
L24 (         4) SEA FILE=HCAPLUS ABB=ON  PLU=ON  L3 AND L23
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search of structure in Registry file
search Registry hits in HCAPLUS
Registry # for glycogen phosphorylase

controlled vocabulary index terms (/ct) that correspond to key words listed on search request form

combined answer set using controlled terms. This is the one I called you about.

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L28 (         2)SEA FILE=HCAPLUS ABB=ON  PLU=ON  WO199639384/PN OR WO199639385/
                  PN
L29 (        91)SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 NOT L28
L30 (    334749)SEA FILE=HCAPLUS ABB=ON  PLU=ON  (((GLYCOGEN/AB (5A) PHOSPHORYL
                  ?/AB (5A) INHIBIT?/AB) OR (DIABET?/AB) OR (CARDIO?/AB OR
                  HEART/AB OR MYOCARDI?/AB) OR (ISCHEMIA/AB (5A) MYOCARD?/AB) OR
                  (REPERFUS?/AB OR RE-PERFUS?/AB))) OR (((GLYCOGEN/TI (5A)
                  PHOSPHORYL?/TI (5A) INHIBIT?/TI) OR (DIABET?/TI) OR (CARDIO?/TI
                   OR HEART/TI OR MYOCARDI?/TI) OR (ISCHEMIA/TI (5A) MYOCARD?/TI)
                   OR (REPERFUS?/TI OR RE-PERFUS?/TI)))
L31           30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L29 AND L30
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remove inventors priority documents

Search free text of abstract (/AB) and title (/TI) with terms listed on search request form.

(final answer set)

=> D IBIB ABS HITSTR 1-30 — print answer set

L31 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:484863 HCAPLUS
DOCUMENT NUMBER: 137:47448
TITLE: Preparation of substituted phenylalaninol derivatives as protein tyrosine phosphatase inhibitors
INVENTOR(S): Larsen, Scott D.; May, Paul D.; Bleasdale, John E.; Liljebris, Charlotta; Schostarez, Heinrich Josef; Barf, Tjeerd; Nilsson, Marianne
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 144 pp., Cont.-in-part of U.S. Ser. No. 138,642.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6410585	B1	20020625	US 1999-265410	19990310
US 6353023	B1	20020305	US 1998-138642	19980824
WO 2000053583	A1	20000914	WO 2000-US6022	20000309
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1161421	A1	20011212	EP 2000-917793	20000309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.:

US 1997-57730P	P	19970828
US 1998-138642	A2	19980824
US 1999-265410	A	19990310
WO 2000-US6022	W	20000309

OTHER SOURCE(S): MARPAT 137:47448
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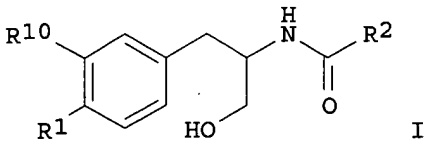
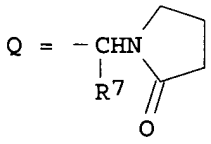


I



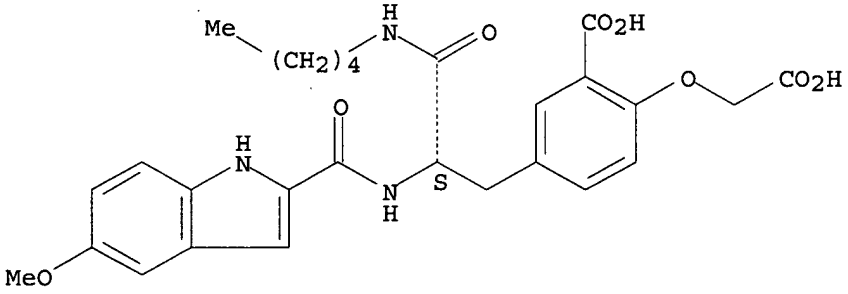
AB The invention comprises phenylalaninol derivs., e.g., I [R1 = OSO3H, OCH(CO2R5)2, OCH2CO2R5, OCH(CO2R5)CH2CO2R5, OC(CO2R5):CHCO2R5, CH2CH(CO2R5)2, CH:C(CO2R5)2, OCH2CONHOH, N(CH2CO2R5)2, OCHFCO2R5 (R5 = H, alkyl, alkylphenyl); R2 = CHR7NHXR6, group Q (R6 = alkyl, alkyl-CONH2, alkyl-NHCO2R5, etc.; R7 = H, any group given for R6); R10 = H, CO2R5, CONHOH, 5-tetrazolyl, F, OCH2CO2R5], or their pharmaceutically acceptable salts, as small mol. wt., non-peptidic inhibitors of protein tyrosine phosphatase 1 (PTP1) which are useful for the treatment and/or prevention of non-insulin dependent **diabetes** mellitus. Thus, 5-[(2S)-2-[[(2S)-2-[(tert-butoxycarbonyl)amino]-3-phenylpropanoyl]amino]-3-hydroxypropyl]-2-(carboxymethoxy)benzoic acid (claimed compd.) was prepd. and showed 80% inhibition of protein tyrosine phosphatase 1B at a concn. of 10 .mu.M.

IT **292833-72-8P 292833-82-0P 292833-93-3P**
292834-05-0P 292834-16-3P 292834-26-5P
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(prepn. of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

RN 292833-72-8 HCAPLUS

CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-2-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-3-oxo-3-(pentylamino)propyl]- (9CI) (CA INDEX NAME)

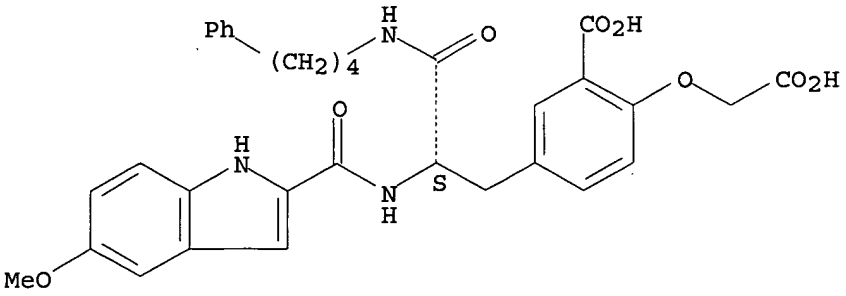
Absolute stereochemistry.



RN 292833-82-0 HCAPLUS

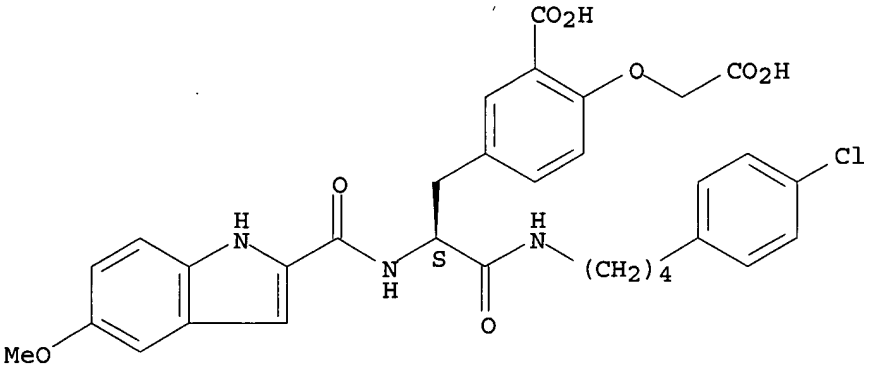
CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-2-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-3-oxo-3-[(4-phenylbutyl)amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



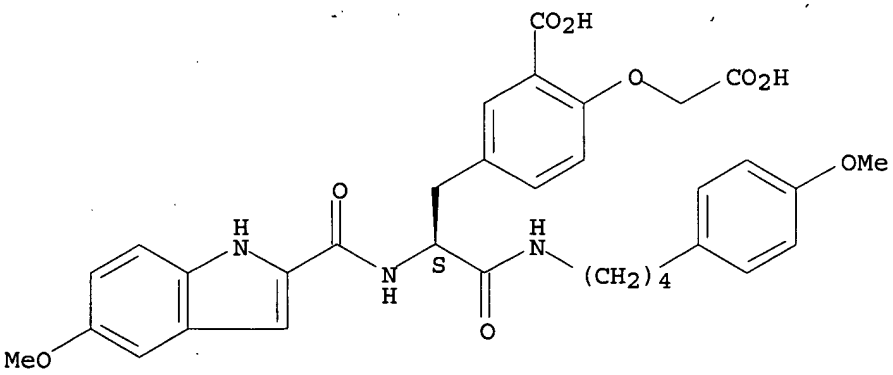
RN 292833-93-3 HCAPLUS
CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-3-[[4-(4-chlorophenyl)butyl]amino]-2-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-3-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 292834-05-0 HCAPLUS
CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-2-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-3-[[4-(4-methoxyphenyl)butyl]amino]-3-oxopropyl]- (9CI) (CA INDEX NAME)

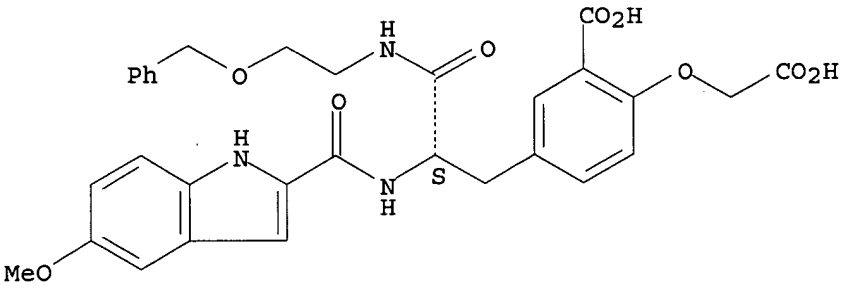
Absolute stereochemistry.



RN 292834-16-3 HCAPLUS
CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-2-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-3-oxo-3-[[2-(phenylmethoxy)ethyl]amino]propyl]- (9CI)

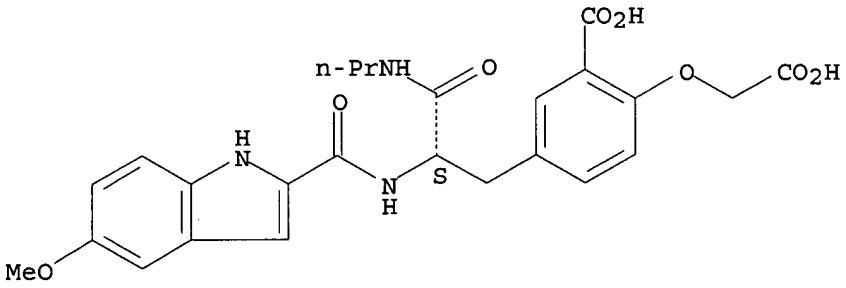
(CA INDEX NAME)

Absolute stereochemistry.



RN 292834-26-5 HCAPLUS
CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-2-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-3-oxo-3-(propylamino)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:309882 HCAPLUS
DOCUMENT NUMBER: 136:325415
TITLE: Preparation of mono- and bis-indolylquinones as GRB-2 adaptor protein inhibitors for treatment of cell proliferative disorders and insulin-related disorders
INVENTOR(S): Tang, Peng Cho; McMahon, Gerald; Harris, G. Davis, Jr.; Lipson, Ken
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 41 pp., Cont.-in-part of U.S. Ser. No. 6,090,838.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6376529	B1	20020423	US 1999-405244	19990924
US 5780496	A	19980714	US 1996-658337	19960605
US 5786488	A	19980728	US 1997-964791	19971105
US 6110957	A	20000829	US 1998-72861	19980505

US 6090838 A 20000718 US 1998-90737 19980604
WO 2001021589 A2 20010329 WO 2000-US26235 20000925
WO 2001021589 A3 20020117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1218342 A2 20020703 EP 2000-965395 20000925
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.:

US 1995-476136	B2	19950607
US 1996-658337	A1	19960605
US 1996-30604P	P	19961113
US 1997-42989P	P	19970414
US 1997-964791	A3	19971105
US 1998-72861	A2	19980505
US 1998-90737	A2	19980604
US 1999-405244	A1	19990924
WO 2000-US26235	W	20000925

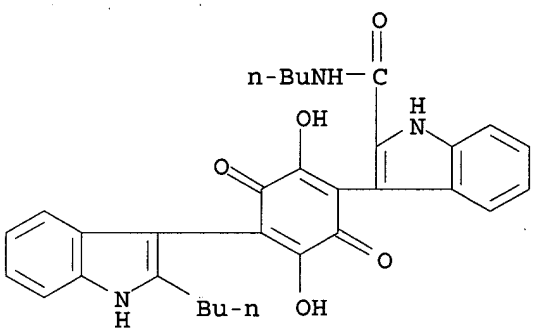
OTHER SOURCE(S): MARPAT 136:325415
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein A = mono- or bicyclic aryl, heteroaryl, (alkyl)carboxy, alkyl(aryl), alkynyl, alkenylcarboxy, hydroxy(alkyl), alkoxy, NO2, halo, trihalomethyl, amido, carboxamido, sulfonyl, sulfonamido, amino, mercapto, or 2-methylbut-2-en-4-yl; R1 and R2 = independently H, halo, OH, or OCOR; R = alkyl(aryl) or aryl; R1a and R2a = independently H, alkyl, alkenyl, alkynyl, or (alkyl)aryl; R3-R6 and R8-R11 = independently H, alkyl(carboxy), alkenyl(carboxy), alkynyl, (alkyl)aryl, hydroxy(alkyl), alkoxy, NO2, halo, trihalomethyl, amido, carboxamido, carboxy, sulfonyl, sulfonamido, amino, mercapto, or 2-methylbut-2-en-4-yl; R12 = H, mono- or bicyclic aryl, heteroaryl, alkyl(carboxy), alkenyl(carboxy), alkynyl, (alkyl)aryl, hydroxy(alkyl), alkoxy, NO2, halo, trihalomethyl, amido, carboxamido, carboxy, sulfonyl, sulfonamido, amino, mercapto, or 2-methylbut-2-en-4-yl; with provisos; or pharmaceutically acceptable salts thereof] were prepd. as GRB-2 adaptor protein inhibitors. I are useful for ameliorating the symptoms of cell proliferative disorders assocd. with CRB-2 adaptor protein function and for treating insulin-related disorders, such as **diabetes**, insulin resistance, insulin deficiency, and insulin allergy. For example, a mixt. of tetrabromo-1,4-benzoquinone, 2-phenylindole, and Cs2CO3 in AcCN was stirred at room temp. for 3 h. Addn. of 2-(3-methylbutyl)indole, stirring at room temp. for 24 h, and heating to 85.degree.C with THF, EtOH, and KOH for 10 h afforded II. The latter effectively bound tyrosine phosphorylated EGF-receptor to a GRB-2 SH2 peptide domain, inhibited A431 vulvar carcinoma tumor cell growth in vivo by 49% at 75 mg/kg/day and 55% at 100 mg/kg/day, gave an EC50 of 6.5 .mu.M in the LDH cytotoxicity assay, and both stimulated phosphorylation of insulin receptor tyrosine kinase and allowed deactivation of the insulin receptor in NIH 3T3 cells.

IT **331632-13-4P**, 3-[2-(N-Butylcarboxamido)indol-3-yl]-6-(2-butylindol-

3-yl)-2,5-dihydroxy-1,4-quinone
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GRB-2 inhibitor; prepn. of indolylquinones as GRB-2 adaptor protein inhibitors for treatment of cell proliferative disorders and insulin-related disorders)
RN 331632-13-4 HCAPLUS
CN 1H-Indole-2-carboxamide, N-butyl-3-[4-(2-butyl-1H-indol-3-yl)-2,5-dihydroxy-3,6-dioxo-1,4-cyclohexadien-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 119 THERE ARE 119 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:170712 HCAPLUS
DOCUMENT NUMBER: 136:365703
TITLE: The 1.76 .ANG. resolution crystal structure of glycogen phosphorylase b complexed with glucose, and CP 320626, a potential antidiabetic drug
AUTHOR(S): Oikonomakos, Nikos G.; Zographos, Spyros E.; Skamnaki, Vicky T.; Archontis, Georgios
CORPORATE SOURCE: Institute of Biological Research and Biotechnology, The National Hellenic Research Foundation, Athens, 11635, Greece
SOURCE: Bioorganic & Medicinal Chemistry (2002), 10(5), 1313-1319
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CP 320626, a potential antidiabetic drug, **inhibits glycogen phosphorylase** (I) in synergism with glucose. To elucidate the structural basis of synergistic inhibition, the authors detd. the crystal structure of muscle I complexed with both glucose and CP 320626 at 1.76 .ANG. resoln., and refined it to a crystallog. R value of 0.211 (Rfree = 0.235). CP 320626 was found to bind at a novel allosteric site, which was .apprx.33 .ANG. from the catalytic site, where glucose binds. The high-resoln. structure allowed unambiguous definition of the conformation of the 1-acetyl-4-hydroxy-piperidine ring supported by theor. energy calcns. Both CP 320626 and glucose promoted the less active T-state, thereby explaining their synergistic inhibition. Structural comparison of the I.cntdot.glucose.cntdot.CP 320626 complex with liver glycogen phosphorylase a (II) complexed with a related compd. (CP 403700)

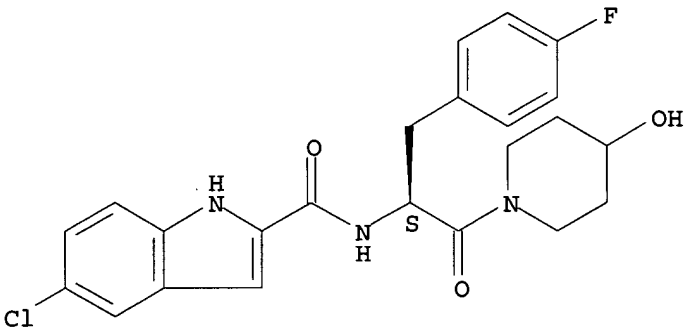
showed that the ligand binding site was conserved in II.

IT **186430-23-9D**, CP 320626, complexes with phosphorylase b and glucose
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(crystal structure of phosphorylase b complexed with glucose and CP 320626, a potential antidiabetic drug)

RN 186430-23-9 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:104618 HCAPLUS
DOCUMENT NUMBER: 136:145214
TITLE: Use of **glycogen phosphorylase inhibitors** to **inhibit** tumor growth
INVENTOR(S): Krasner, Alan Seth
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1177791	A2	20020206	EP 2001-306440	20010727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002128673	A2	20020509	JP 2001-226129	20010726
US 2002123513	A1	20020905	US 2001-919205	20010731

PRIORITY APPLN. INFO.: US 2000-221717P P 20000731
OTHER SOURCE(S): MARPAT 136:145214

AB The invention relates to the use of **glycogen phosphorylase inhibitors** to **inhibit** abnormal cell growth in mammals, including humans. The invention also relates to pharmaceutical compns. contg. **glycogen phosphorylase inhibitors** alone or in combination with other **glycogen phosphorylase inhibitors** or other **inhibitors** of abnormal cell growth, and to methods of treating cancer,

hyperproliferative disorders, or abnormal cell growth in a mammal by administering to a mammal in need thereof the compds. and compns. of the invention.

IT **9012-69-5P**, Glycogen phosphorylase B
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(glycogen phosphorylase **inhibitor** to **inhibit** tumor growth)
RN 9012-69-5 HCAPLUS
CN Phosphorylase b (9CI) (CA INDEX NAME)

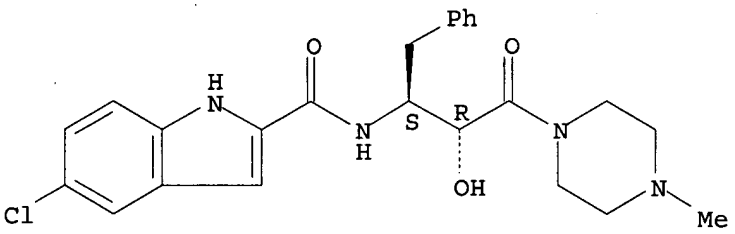
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **9035-74-9P**, Glycogen phosphorylase
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(glycogen phosphorylase **inhibitor** to **inhibit** tumor growth)
RN 9035-74-9 HCAPLUS
CN Phosphorylase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **186392-09-6 186392-46-1 186392-47-2**
186392-51-8 186392-52-9 186392-53-0
186392-64-3 186429-66-3 186430-04-6
186430-23-9 186430-40-0 186431-27-6
186431-28-7 208830-24-4 208830-25-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycogen phosphorylase inhibitor to inhibit tumor growth)
RN 186392-09-6 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(4-methyl-1-piperazinyl)-3-oxo-1-(phenylmethyl)propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

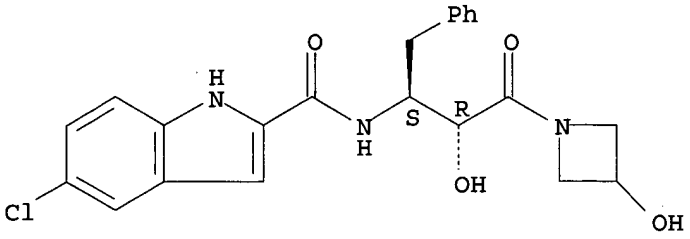
Absolute stereochemistry.



● HCl

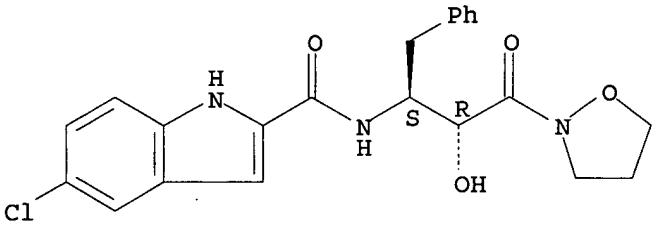
RN 186392-46-1 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(3-hydroxy-1-azetidinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



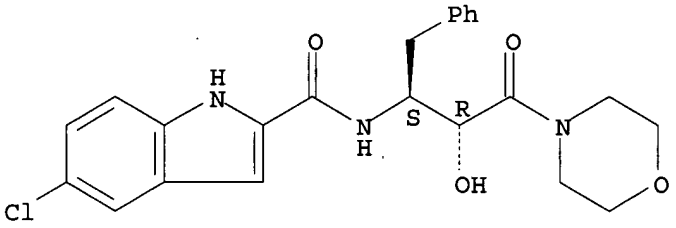
RN 186392-47-2 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(2-isoxazolidinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



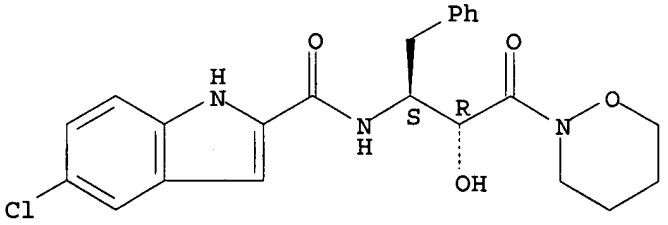
RN 186392-51-8 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(4-morpholinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



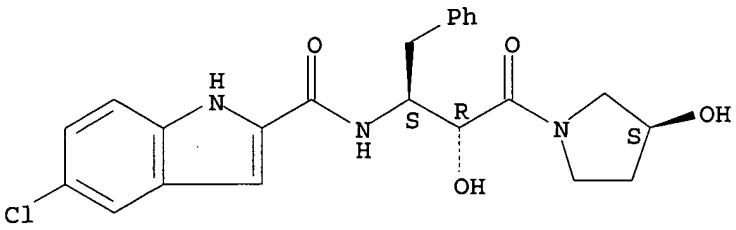
RN 186392-52-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-oxo-1-(phenylmethyl)-3-(tetrahydro-2H-1,2-oxazin-2-yl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



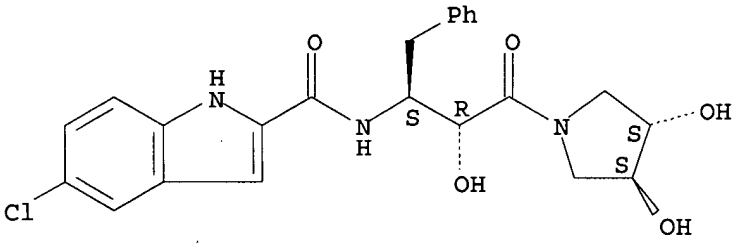
RN 186392-53-0 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(3S)-3-hydroxy-1-pyrrolidinyl]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

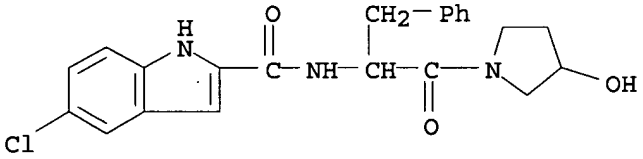


RN 186392-64-3 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

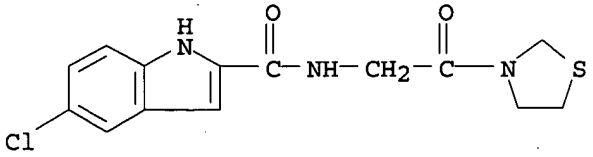
Absolute stereochemistry.



RN 186429-66-3 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-(3-hydroxy-1-pyrrolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

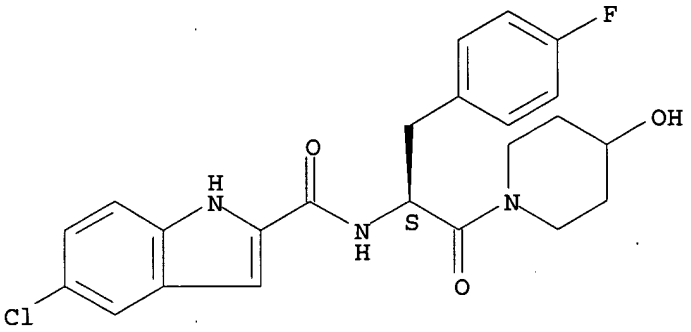


RN 186430-04-6 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-oxo-2-(3-thiazolidinyl)ethyl]- (9CI) (CA INDEX NAME)



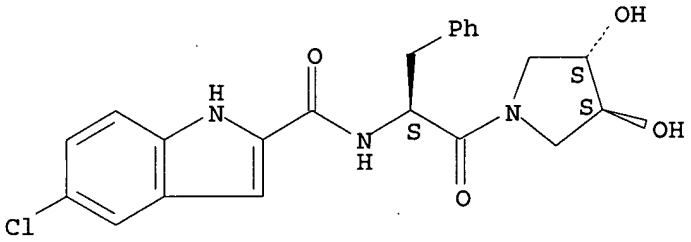
RN 186430-23-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



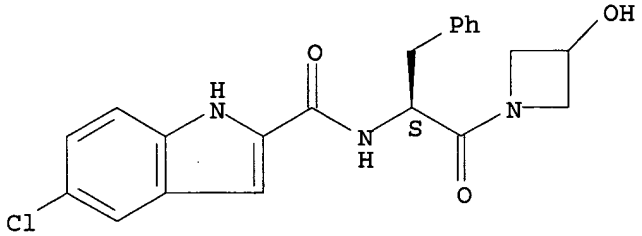
RN 186430-40-0 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



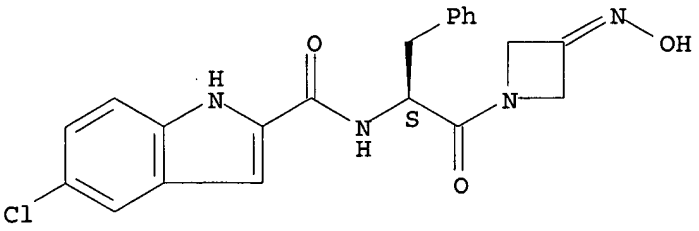
RN 186431-27-6 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-azetidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



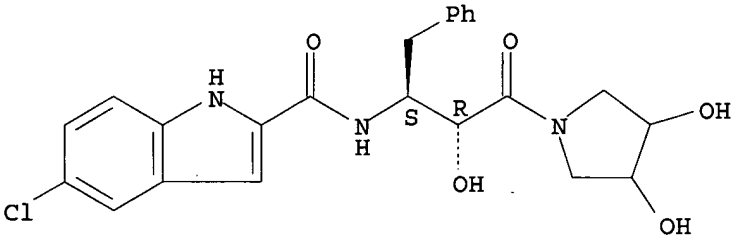
RN 186431-28-7 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[3-(hydroxyimino)-1-azetidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



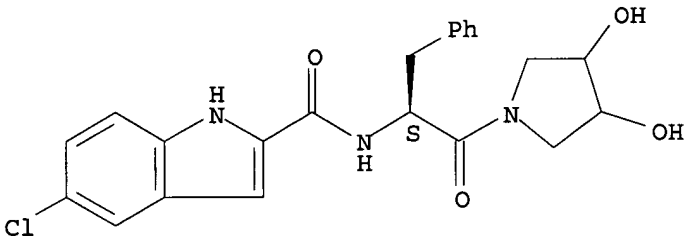
RN 208830-24-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(3,4-dihydroxy-1-pyrrolidinyl)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 208830-25-5 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3,4-dihydroxy-1-pyrrolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



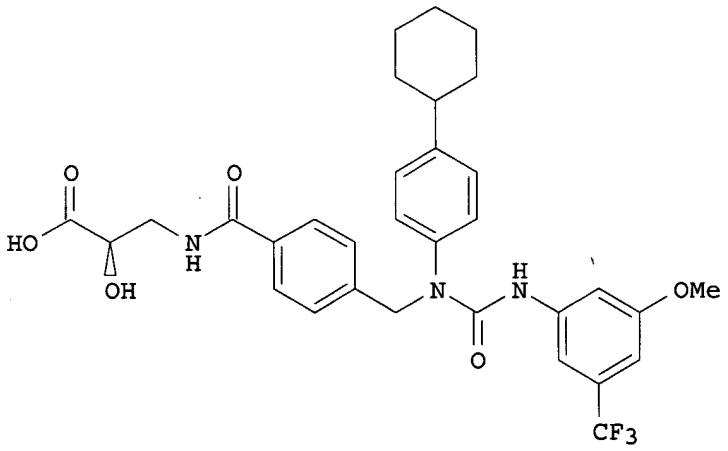
L31 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:10432 HCAPLUS
DOCUMENT NUMBER: 136:85669
TITLE: Preparation of (e.g.) N-alkylaryl-N-aryl-N'-aryl ureas as glucagon antagonists/inverse agonists
INVENTOR(S): Jorgensen, Anker Steen; Christensen, Inge Thoger; Kodra, Janos Tibor; Madsen, Peter; Behrens, Carsten; Sams, Christian; Lau, Jesper
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000612	A1	20020103	WO 2001-DK435	20010621
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001065834	A5	20020108	AU 2001-65834	20010621

PRIORITY APPLN. INFO.:
DK 2000-984 A 20000623
DK 2000-1734 A 20001117
WO 2001-DK435 W 20010621

OTHER SOURCE(S): MARPAT 136:85669
GI



II

AB Title compds. R1OC(O)-A-CR2R3-N(R4)-C(O)-Z-CHR5-N(E)-X-D [R1-5 = H, alkyl; A = C(O), CH-alkoxy, CHF; Z = (un)substituted arylene or a divalent radical derived from a 5 or 6 membered heteroarom. ring contg. 1 or 2 heteroatoms selected from N, O and S; X = alkyl, acyl, amido, etc.; D = (un)substituted Ph, naphthyl, pyridyl, benzothiophenyl, etc.; E = (un)substituted cyclohexyl, Ph, benzyl, phenethyl, etc.; I] were prepd. Examples include data for 73 compds., two glucagon receptor binding assays and a glucose-dependent insulinotropic peptide (GIP) receptor binding assay. E.g., 4-cyclohexylaniline was reductively alkylated with 4-formyl benzoic acid Me ester (MeOH, HOAc, NaCNBH3) in 87% yield. The amine was added to an isocyanate derived from 5-methoxy-3-trifluoromethylaniline (prepn. given; CH2Cl2, room temp.) to give a urea as an oil that was sapond. (EtOH, NaOH, room temp., 16 h) to give the solid carboxylic acid in 49% yield. The carboxylic acid was coupled to (R)-isoserine Et ester (DMF, HOBt, EDAC) followed by hydrolysis to give example compd. II as a cryst. solid. In a glucagon receptor binding assay, compds. of the

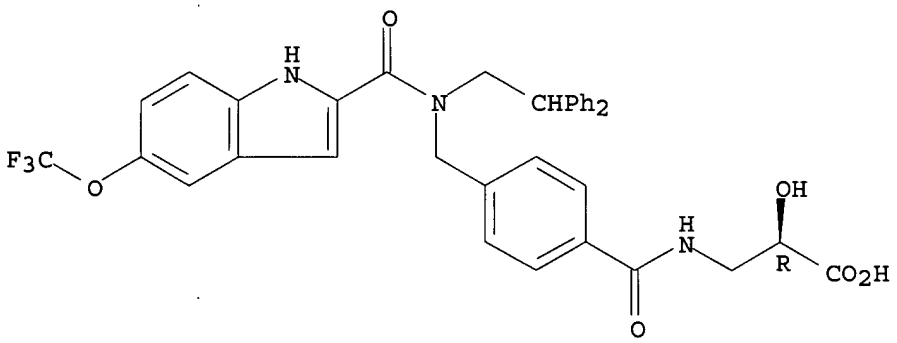
invention had IC50 < 1500 nM and many were below 250 nM. I are useful in the treatment or prevention of any diseases wherein a glucagon antagonistic action is beneficial, such as hyperglycemia, type 1 **diabetes**, type 2 **diabetes**, disorders of lipid metab. and obesity.

IT **385836-75-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; prepn. of N-alkylaryl-N-aryl-N'-aryl ureas as glucagon antagonists/inverse agonists)

RN 385836-75-9 HCAPLUS

CN Propanoic acid, 3-[[4-[[(2,2-diphenylethyl)[[5-(trifluoromethoxy)-1H-indol-2-yl]carbonyl]amino]methyl]benzoyl]amino]-2-hydroxy-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

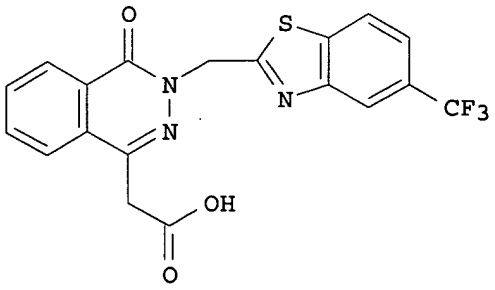


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

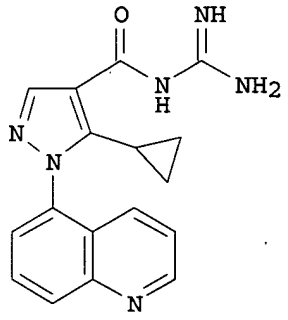
L31 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:936092 HCAPLUS
DOCUMENT NUMBER: 136:53752
TITLE: Synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors
INVENTOR(S): Mylari, Banavara L.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 41 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001056095	A1	20011227	US 2001-782798	20010213

PRIORITY APPLN. INFO.: US 2000-183004P P 20000216
GI



I



II

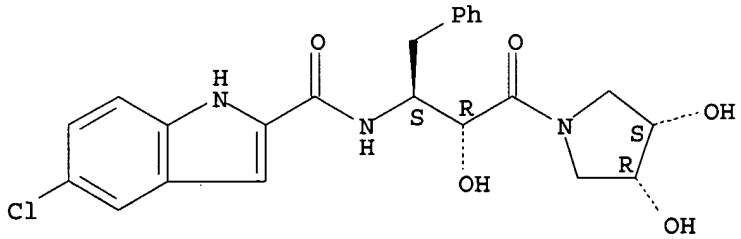
AB Mono-, di- and triethanolamine salts of [4-Oxo-(5-trifluoromethylbenzothiazol-2-ylmethyl)-3,4-dihydrophthalazin-1-yl]acetic acid (zopolrestat; I) were prepd. E.g., a soln. of I in acetone was added to ethanolamine (10 mol equiv, room temp., 1 h) which afforded, after purifn., the ethanolamine salt in 95% yield, m.p. 119 - 121.degree.C. Ethanolamine salts of I are used alone or with NHE-1 inhibitors (e.g. II), selective serotonin reuptake **inhibitors** (SSRIs, e.g. fluoxetine), **glycogen phosphorylase inhibitors** (GPIs), sorbitol dehydrogenase **inhibitors** (SDIs) and antihypertensive agents for treating **diabetic** complications.

IT **186392-65-4**
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(combination pharmaceutical; synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors)

RN 186392-65-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



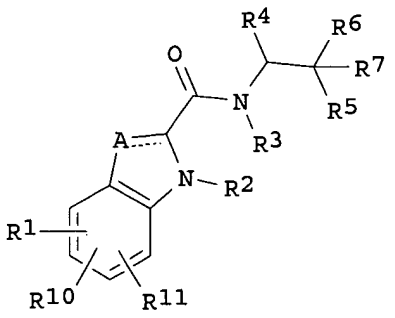
IT **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 **inhibitors**)
RN 9035-74-9 HCAPLUS
CN Phosphorylase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

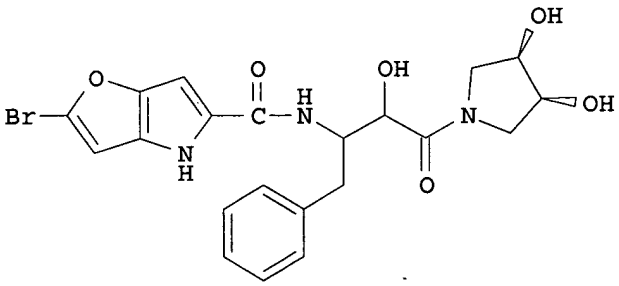
L31 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:709687 HCAPLUS
DOCUMENT NUMBER: 135:272869
TITLE: Synthesis of indolyl-amides as **glycogen phosphorylase inhibitors** for treatment of type 2 **diabetes**
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136071	A2	20010926	EP 2001-301979	20010305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001302546	A2	20011031	JP 2001-78839	20010319

PRIORITY APPLN. INFO.: US 2000-191381P P 20000322
OTHER SOURCE(S): MARPAT 135:272869
GI



I



II

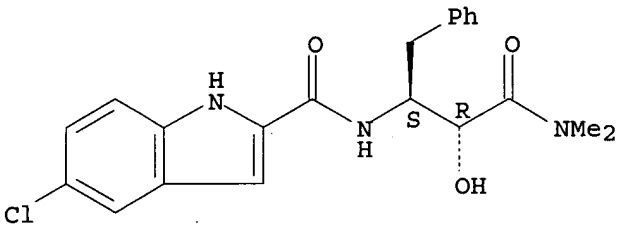
AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH2, CH-alkyl when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6- or 7-NO2, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R2 = H; R3 = H, alkyl; R4 = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R5 = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R7 = H, F, alkyl; or R5 and R7 can be taken together to be oxo; R6 = carboxy, alkoxycarbonyl, amido, acyl, alkyl, OH, alkoxy; R9 = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and derivs. were prepd. Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydroxypyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF, HOBt, EDC, room temp.) to give amide II. Compds. I are **glycogen phosphorylase inhibitors** used for treating type 2 **diabetes** mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-**glycogen phosphorylase inhibiting** anti-**diabetic** agents are also claimed.

IT **186392-40-5P 186392-46-1P 186392-47-2P**
186392-49-4P 186392-51-8P 186392-52-9P
186392-53-0P 186392-64-3P 186392-65-4P
186392-70-1P 186429-64-1P 186429-91-4P
186430-03-5P 186430-23-9P 186430-41-1P
186430-83-1P 186431-27-6P 186431-28-7P
186431-29-8P 225929-30-6P 362521-64-0P
362521-65-1P 362521-66-2P 362521-89-9P
362521-91-3P
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

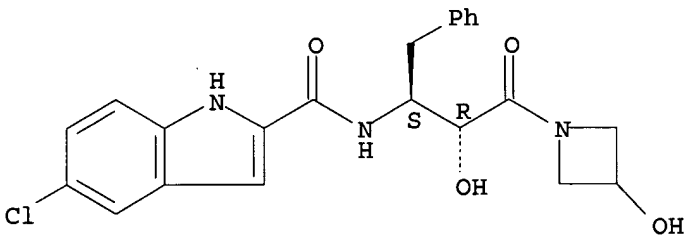
RN 186392-40-5 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



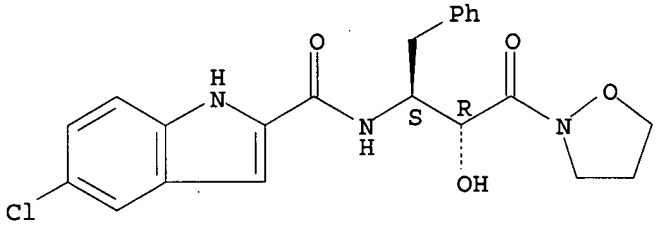
RN 186392-46-1 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(3-hydroxy-1-azetidinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



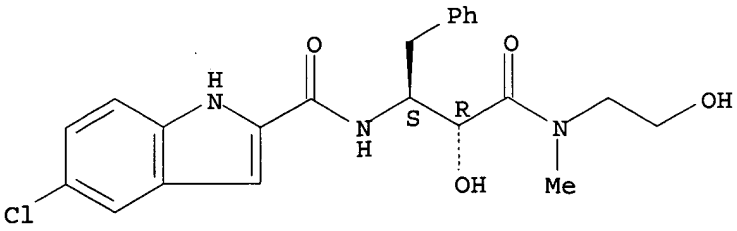
RN 186392-47-2 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(2-isoxazolidinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



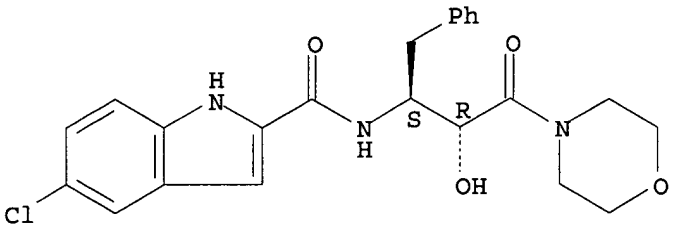
RN 186392-49-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(2-hydroxyethyl)methylamino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



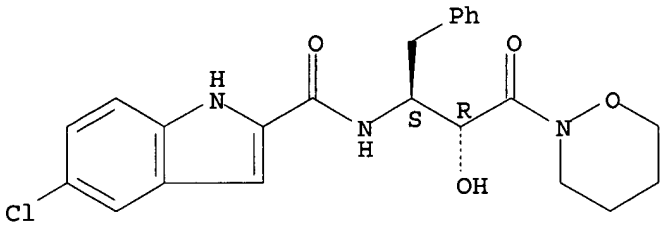
RN 186392-51-8 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(4-morpholinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



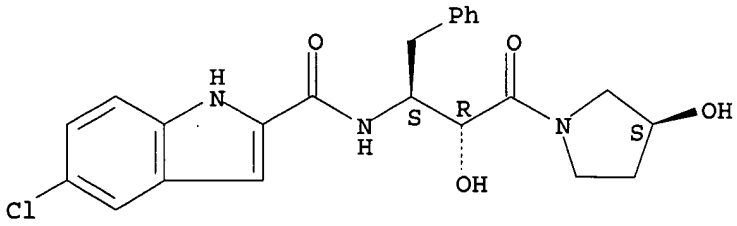
RN 186392-52-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-oxo-1-(phenylmethyl)-3-(tetrahydro-2H-1,2-oxazin-2-yl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



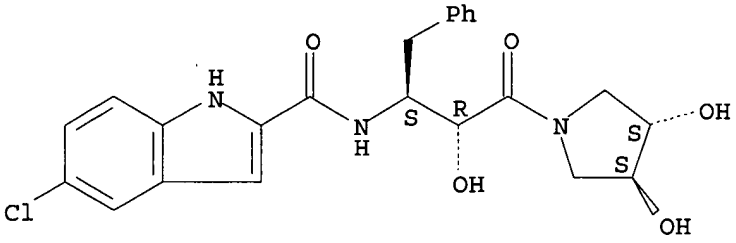
RN 186392-53-0 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(3S)-3-hydroxy-1-pyrrolidinyl]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



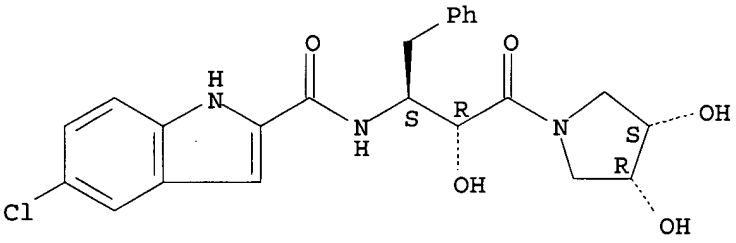
RN 186392-64-3 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



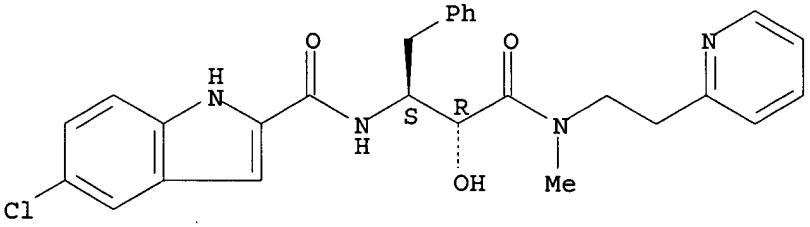
RN 186392-65-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



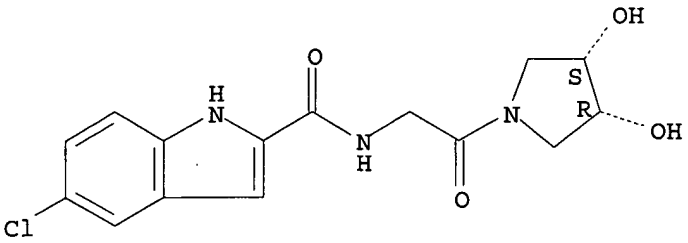
RN 186392-70-1 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[methyl[2-(2-pyridinyl)ethyl]amino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



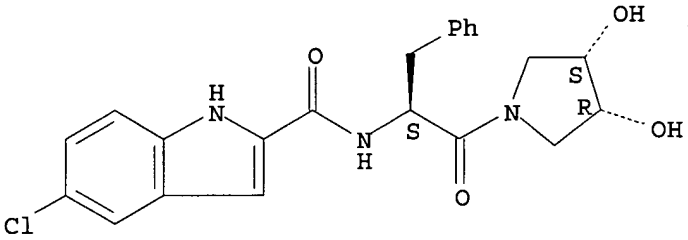
RN 186429-64-1 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxoethyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

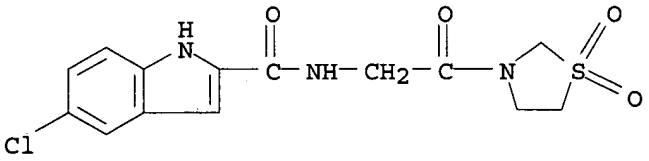


RN 186429-91-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[(3S,4R)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

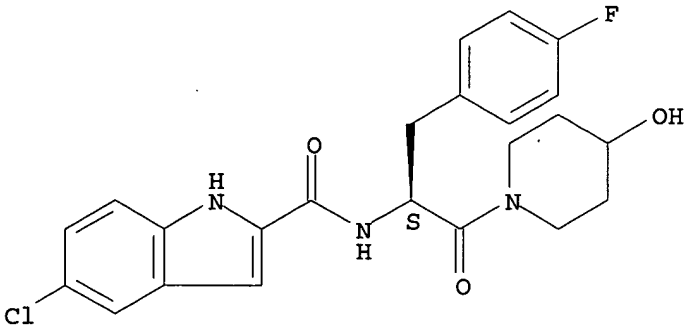


RN 186430-03-5 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-(1,1-dioxido-3-thiazolidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)



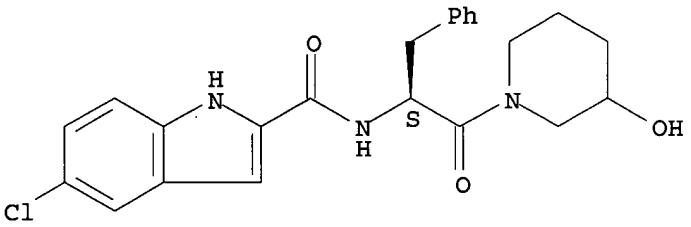
RN 186430-23-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



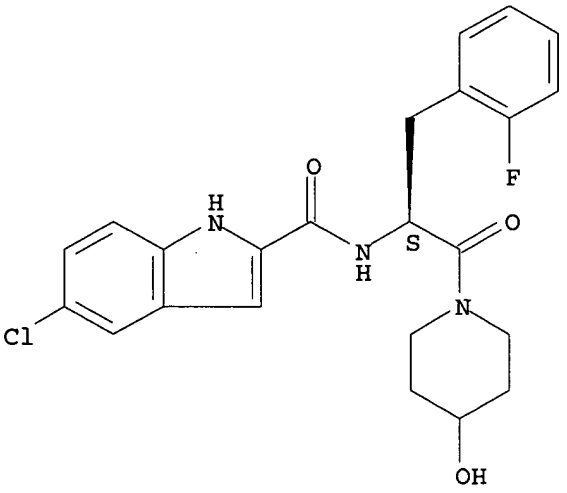
RN 186430-41-1 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-piperidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



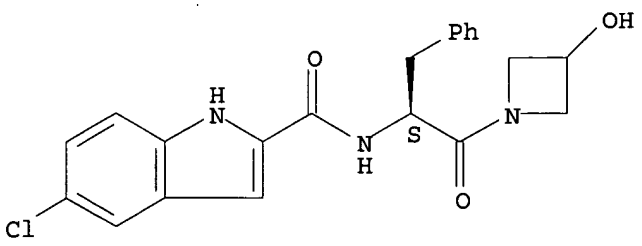
RN 186430-83-1 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(2-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



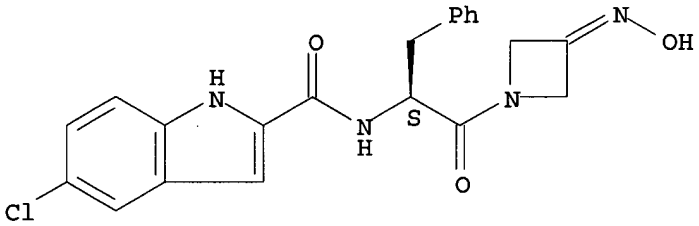
RN 186431-27-6 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-azetidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



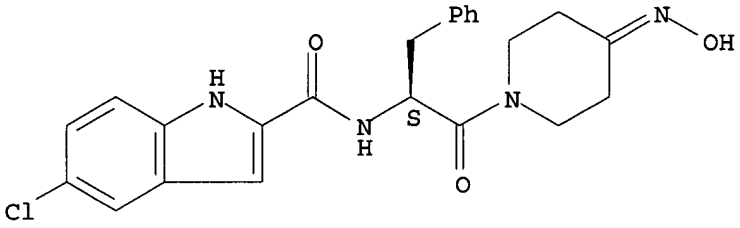
RN 186431-28-7 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[3-(hydroxyimino)-1-azetidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



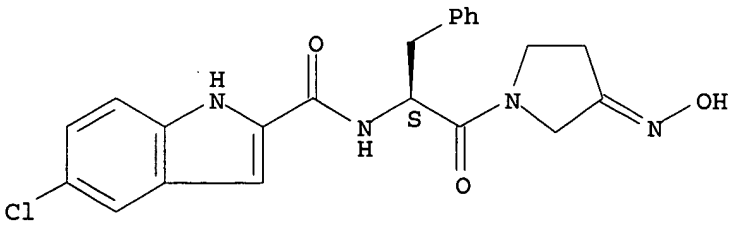
RN 186431-29-8 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[4-(hydroxyimino)-1-piperidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



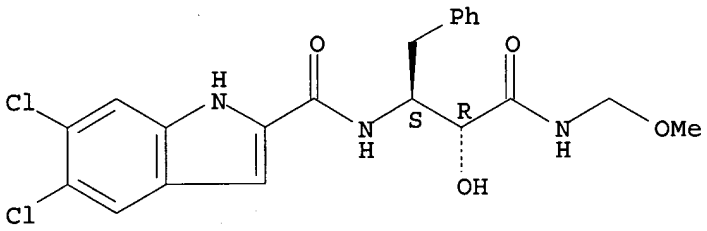
RN 225929-30-6 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[3-(hydroxyimino)-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



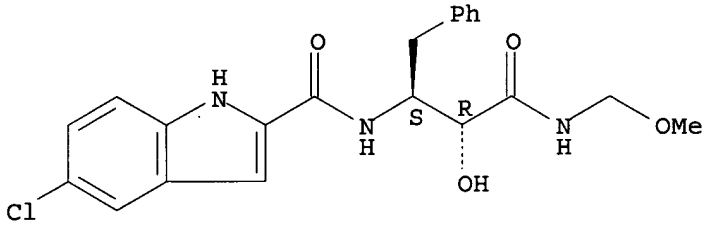
RN 362521-64-0 HCAPLUS
CN 1H-Indole-2-carboxamide, 5,6-dichloro-N-[(1S,2R)-2-hydroxy-3-[(methoxymethyl)amino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



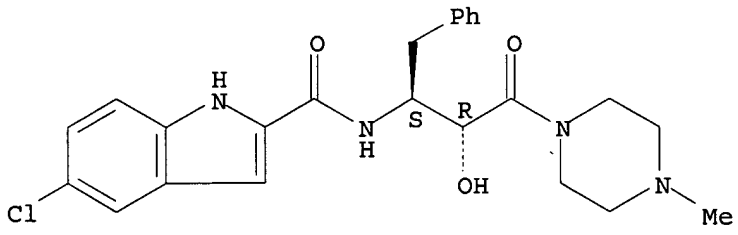
RN 362521-65-1 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(methoxymethyl)amino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

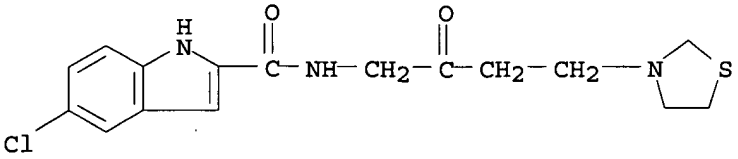


RN 362521-66-2 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(4-methyl-1-piperazinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

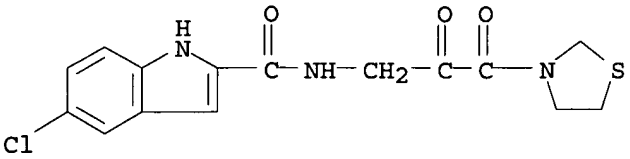
Absolute stereochemistry.



RN 362521-89-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-oxo-4-(3-thiazolidinyl)butyl]- (9CI) (CA INDEX NAME)



RN 362521-91-3 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2,3-dioxo-3-(3-thiazolidinyl)propyl]-(9CI) (CA INDEX NAME)



IT **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(synthesis of indolyl-amides as glycogen phosphorylase **inhibitors** for treatment of type 2 diabetes)
RN 9035-74-9 HCAPLUS
CN Phosphorylase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

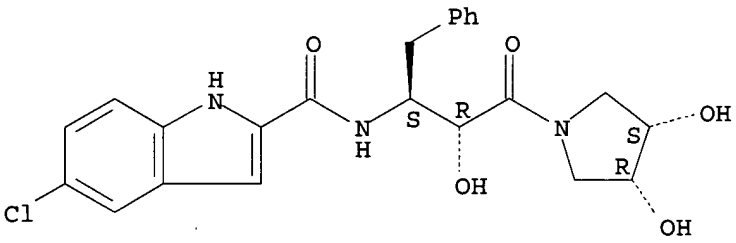
L31 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:693088 HCAPLUS
DOCUMENT NUMBER: 135:262225
TITLE: **Glycogen phosphorylase inhibitor** compositions
INVENTOR(S): Babcock, Walter C.; Friesen, Dwayne Thomas; Lorenz, Douglas Alan; Macri, Christopher A.; Nightingale, James Alan Schriver; Shanker, Ravi Mysore; Hancock, Bruno Caspar; Crew, Marshall D.
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068092	A2	20010920	WO 2001-IB389	20010316
WO 2001068092	A3	20020321		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 2001053791 A1 20011220 US 2001-808559 20010314
PRIORITY APPLN. INFO.: US 2000-190125P P 20000316
AB Pharmaceutical compns. of a particularly effective sparingly sol. **glycogen phosphorylase inhibitor** are disclosed. Thus, an amorphous solid dispersion contg. 25% a drug and 75% polymer was made by first mixing the drug in acetone together with a finely powd. HPMCAS to form a soln. The soln. comprised 1.25% drug, 3.75% HPMCAS, and 95% acetone. This soln. was then spray-dried by directing an atomizing spray via a 2-fluid external mix spray nozzle at 2.6 bar at a 175 to 180 g/min feed rate into a stainless steel chamber of a NIRO XP spray drier, maintained at a temp. of 180.degree. at the inlet and 69.degree. at the outlet.
IT **186392-65-4**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(glycogen phosphorylase inhibitor compns.)
RN 186392-65-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitor**; glycogen phosphorylase **inhibitor** compns.)
RN 9035-74-9 HCAPLUS
CN Phosphorylase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:693054 HCAPLUS
DOCUMENT NUMBER: 135:247221
TITLE: Pharmaceutical compositions containing **glycogen phosphorylase inhibitors**
INVENTOR(S): Hoover, Dennis Jay; Shanker, Ravi Mysore; Friesen, Dwayne Thomas; Lorenz, Douglas Alan; Nightingale, James Alan Schriver
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 142 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068055	A1	20010920	WO 2001-IB394	20010316
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001053778	A1	20011220	US 2001-805828	20010314

PRIORITY APPLN. INFO.: US 2000-189942P P 20000316

OTHER SOURCE(S): MARPAT 135:247221

AB Pharmaceutical compns. comprise a **glycogen phosphorylase inhibitor** and at least one concn.-enhancing polymer. The compn. may be a simple phys. mixt. of **glycogen phosphorylase inhibitor** and concn.-enhancing polymer or a dispersion of **glycogen phosphorylase inhibitor** and polymer. A dispersion of 25% 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3R,4S)-dihydroxypyrrolidin-1-yl)-3-oxypropyl]amide and 75% polymer was made by first mixing the drug in acetone together with HPMCAS to form a soln. The soln. comprised 1.25 drug, 3.75% HPMCAS, and 95% acetone. This soln. was then spray-dried by directing an atomizing spray using a 2-fluid external-mix spray nozzle at 2.6 bar at a feed rate of 175 to 180 g/min into the stainless-steel chamber of a spray-dryer, maintained at 180.degree. on the inlet and 69.degree. at the outlet. The resulting amorphous solid spray-dried dispersion was collected and then dried in a solvent tray-dryer by spreading the spray-dried particles onto polyethylene-lined trays to a depth of not >1 cm and then drying them at 40.degree. for at least 8 h.

IT **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**inhibitors**; pharmaceutical compns. contg. glycogen phosphorylase **inhibitors**)

RN 9035-74-9 HCAPLUS

CN Phosphorylase (9CI) (CA INDEX NAME)

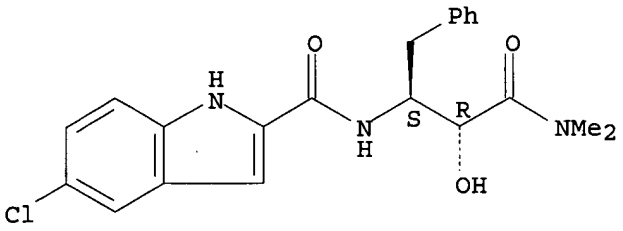
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **186392-40-5 186392-43-8 186392-51-8 186392-53-0 186392-63-2 186392-65-4 186429-91-4 186430-03-5 186430-23-9 186430-40-0 186430-57-9 186431-27-6 361176-31-0**
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

RN 186392-40-5 HCAPLUS

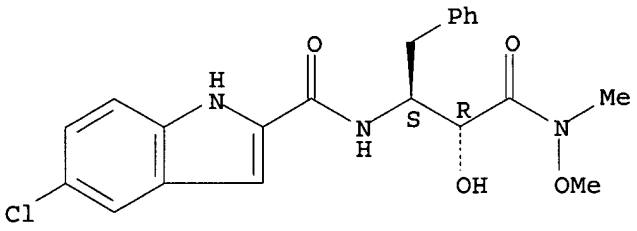
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



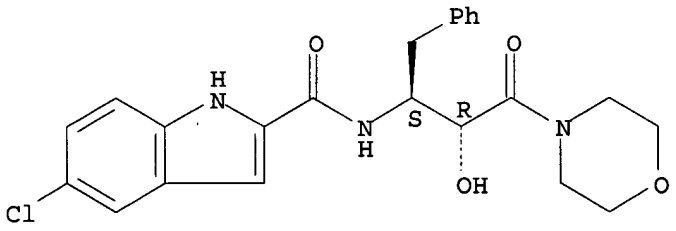
RN 186392-43-8 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



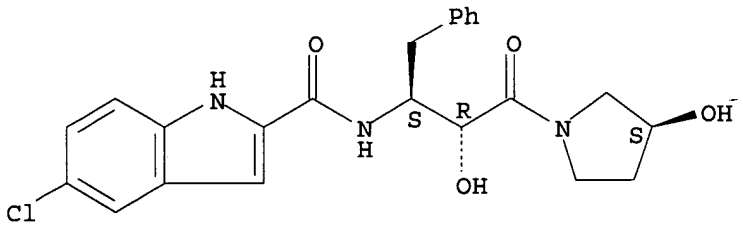
RN 186392-51-8 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(4-morpholinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186392-53-0 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(3S)-3-hydroxy-1-pyrrolidinyl]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

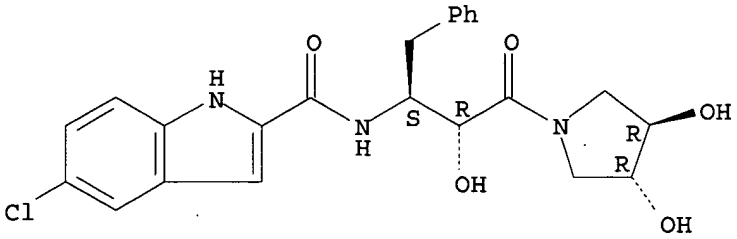
Absolute stereochemistry.



RN 186392-63-2 HCAPLUS

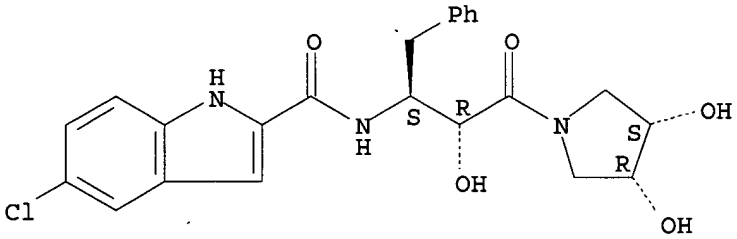
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4R)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



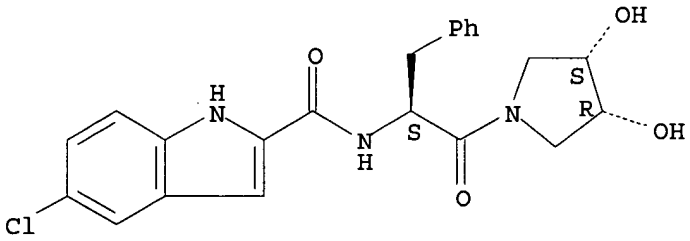
RN 186392-65-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

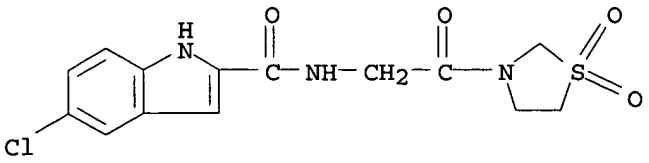


RN 186429-91-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[(3S,4R)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

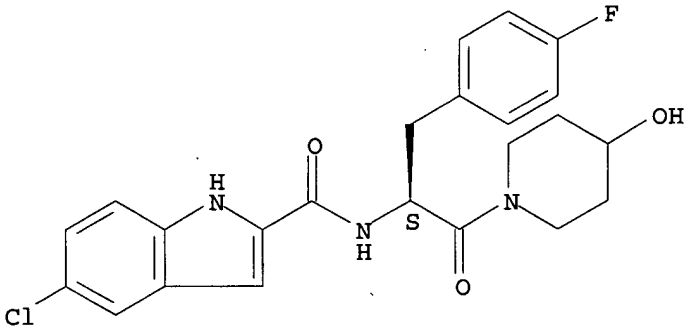


RN 186430-03-5 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-(1,1-dioxido-3-thiazolidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)



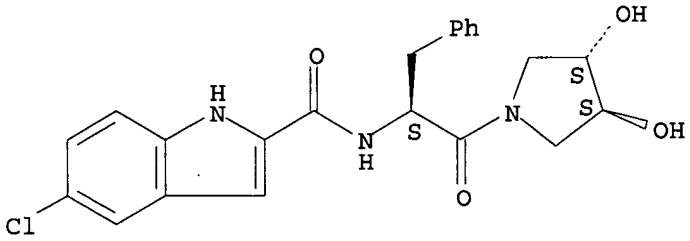
RN 186430-23-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

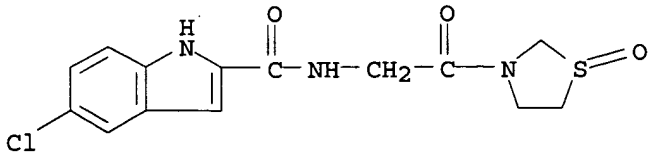


RN 186430-40-0 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



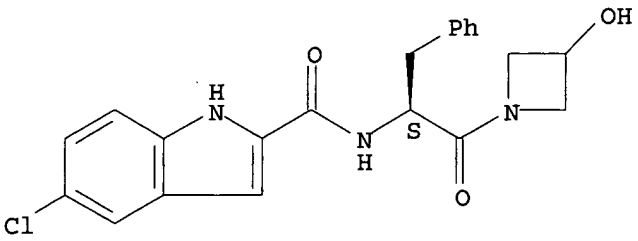
RN 186430-57-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-(1-oxido-3-thiazolidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 186431-27-6 HCAPLUS

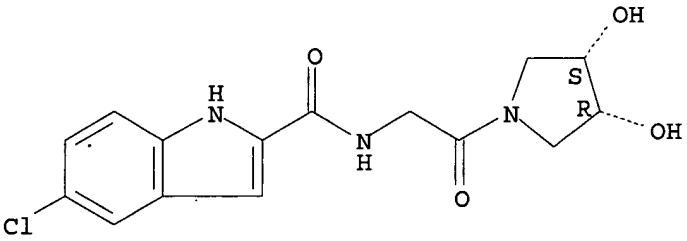
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-azetidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 361176-31-0 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-[(3S,4R)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:554794 HCAPLUS
DOCUMENT NUMBER: 135:132447
TITLE: Chloroindolephenylethylamide analogs and their prodrugs as **glycogen phosphorylase inhibitors** for treatment of **diabetic cardiomyopathy**
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123

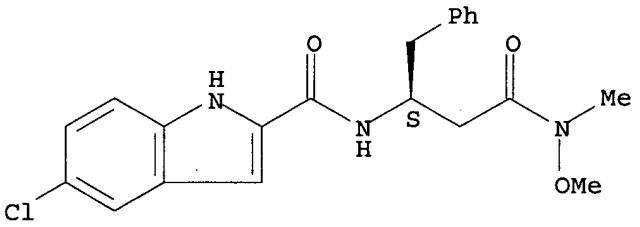
PRIORITY APPLN. INFO.: US 2000-177770P P 20000124
AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-

carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylmethyl)-2-phenylethyl]amide, etc., and their prodrugs are claimed as **glycogen phosphorylase inhibitors** for treatment of **diabetic cardiomyopathy**. The title compds. can also combine with insulin, insulin analogs (biguanides), .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma. agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors, .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid receptor antagonists, and/or thyroid hormone analogs for treatment of **diabetes**, **cardiovascular** diseases, **heart** ischemia, congestive **heart** failure, hypertension, **diabetic** angiopathy, **myocardial** infarction, etc.

IT **186392-21-2 186392-39-2 186392-40-5 186392-49-4 186392-65-4 186392-67-6 186392-70-1**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

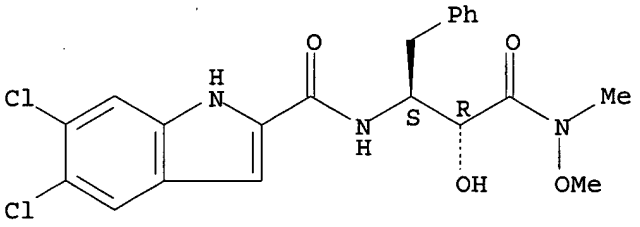
RN 186392-21-2 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



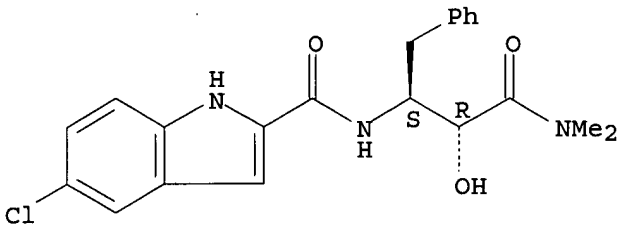
RN 186392-39-2 HCAPLUS
CN 1H-Indole-2-carboxamide, 5,6-dichloro-N-[(1S,2R)-2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



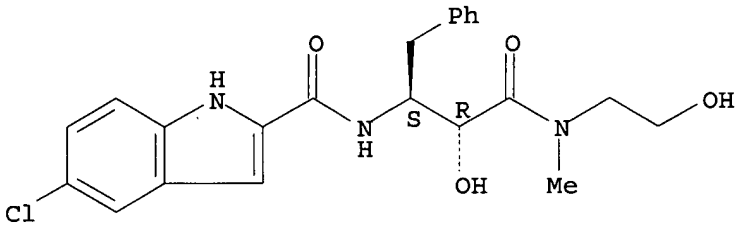
RN 186392-40-5 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



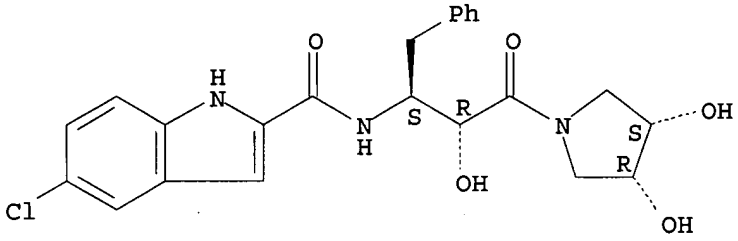
RN 186392-49-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(2-hydroxyethyl)methylamino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



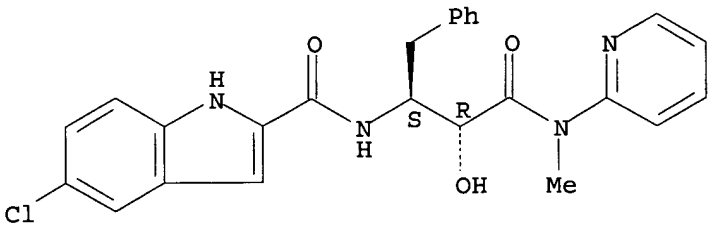
RN 186392-65-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



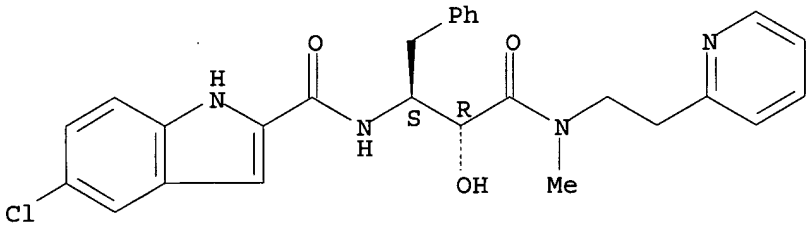
RN 186392-67-6 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methyl-2-pyridinylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186392-70-1 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[methyl[2-(2-pyridinyl)ethyl]amino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase **inhibitors** for treatment of diabetic cardiomyopathy and other cardiovascular diseases)
RN 9035-74-9 HCAPLUS
CN Phosphorylase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:435041 HCAPLUS
DOCUMENT NUMBER: 135:33431
TITLE: Preparation of cycloamine as CCR5 receptor antagonists
INVENTOR(S): Shiota, Tatsuki; Yokoyama, Tomonori; Kamimura, Takashi
PATENT ASSIGNEE(S): Teijin Limited, Japan
SOURCE: PCT Int. Appl., 271 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

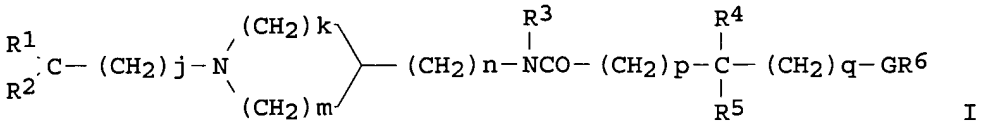
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042208	A1	20010614	WO 2000-JP8627	20001206

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,

YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 1999-348778 A 19991208
OTHER SOURCE(S): MARPAT 135:33431

GI



I

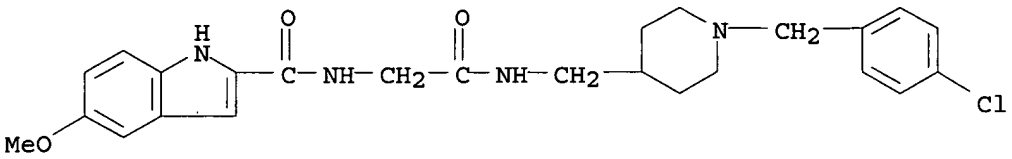
AB Therapeutic or preventive agents for .beta.-chemokine receptor CCR5-related diseases such as AIDS, rheumatoid arthritis, and nephritis, contg. as the active ingredient, cyclic amine derivs. such as piperidine and pyrrolidine derivs. of general formula [I; R1 = (un)substituted Ph, C3-8 cycloalkyl, or arom. heterocyclyl contg. 1-3 heteroatoms of O, S, and/N wherein Ph and arom. heterocyclyl group is optionally condensed to benzene ring or heterocyclyl ring contg. 1-3 heteroatoms of O, S, and/N to from an (un)substituted condensed ring; R2 = H, (un)substituted C1-6 alkyl or Ph, C2-7 alkoxycarbonyl, HO; j, k = 0-2; m = 2-4; n = 0,1; R3 = H, (un)substituted phenyl-optionally substituted C1-6 alkyl; R4, R5 = H, HO, Ph, (un)substituted C1-6 alkyl; or R4 and R5 together represent a 3-6-membered ring cyclic hydrocarbyl; p, q = 0,1; G = CO, SO2, CO2, NR7CO, CONR7, NHCONH, NHC(S)NH, NR7SO2, SO2 NR7, NHCO2, O2CNH (wherein R7 = H, C1-6 alkyl; or R7 and R5 together form C2-5 alkylene); R6 = (un)substituted C3-8 cycloalkyl, C3-6 cycloalkenyl, Ph, benzyl, or arom. heterocyclyl contg. 1-3 heteroatoms of O, S, and/N, wherein Ph, benzyl, and arom. heterocyclyl are optionally condensed with benzene ring or arom. heterocyclyl group contg. 1-3 heteroatoms of O, S, and/N to form an (un)substituted condensed ring], pharmaceutically acceptable adducts of the same with acids, or pharmaceutically acceptable adducts thereof with C1-6 alkyl, are described. Above CCR5-related diseases include diseases accompanied by destruction of cartilage or bone (in particular chronic rheumatoid arthritis), nephritis or kidney diseases (in particular glomerulonephritis, interstitial nephritis, or nephrosis), demyelinating diseases (in particular multiple sclerosis), post-transplant rejection, host-vs.-graft diseases (GVHD), **diabetes**, chronic obstructive pulmonary diseases (COPD), bronchial asthma, atopic dermatitis, sarcoidosis, fibrosis, arteriosclerosis, psoriasis, and inflammatory bowel diseases. Thus, 3-(trifluoromethylthio)benzoic acid was condensed with (R)-1-(4-chlorobenzyl)-3-(glycylamino)pyrrolidine using diisopropylcarbodiimide and HOBt in tert-butanol and CHCl3 at room temp. for 15 h to give (R)-1-(4-chlorobenzyl)-3-[[N-(3-(trifluoromethylthio)benzoyl)glycyl]amino]pyrrolidine (II). II and (R)-1-(6-methyl-3-indolylmethyl)-3-[[N-(2-amino-5-(trifluoromethoxy)benzoyl)glycyl]amino]pyrrolidine 10 .mu.M in vitro inhibited by 20-50% and >80%, resp., the binding of [125I]macrophage inflammatory protein-1.alpha. (MIP-1.alpha.) to CCR5-receptor expressed in CHO cells.

IT **226238-52-4P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of cycloamine as CCR5 receptor antagonists for therapeutics or remedies of .beta.-chemokine receptor CCR5-related diseases such as AIDS, rheumatoid arthritis, and nephritis)

RN 226238-52-4 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-2-oxoethyl]-5-methoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:228870 HCAPLUS

DOCUMENT NUMBER: 134:262851

TITLE: Isoxazoline derivative caspase inhibitors for pharmaceutical uses

INVENTOR(S): Kim, Eunice Eun-Kyeong; Park, Mi-Jeong; Lee, Tae-Hee; Chang, Hye-Kyung; Park, Tae-Kyo; Kang, Chang-Yuil; Kim, Young-Myeong; Moon, Kwang-Yul; Oh, Young-Leem; Min, Chang-Hee; Chung, Hyun Ho

PATENT ASSIGNEE(S): LG Chemical Ltd., S. Korea

SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

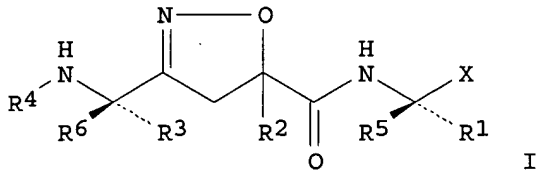
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021600	A1	20010329	WO 2000-KR1047	20000918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2001021599	A1	20010329	WO 1999-KR561	19990917
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1212309	A1	20020612	EP 2000-961242	20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.: WO 1999-KR561 A 19990917
KR 1999-48608 A 19991104
WO 2000-KR1047 W 20000918
OTHER SOURCE(S): MARPAT 134:262851
GI



I

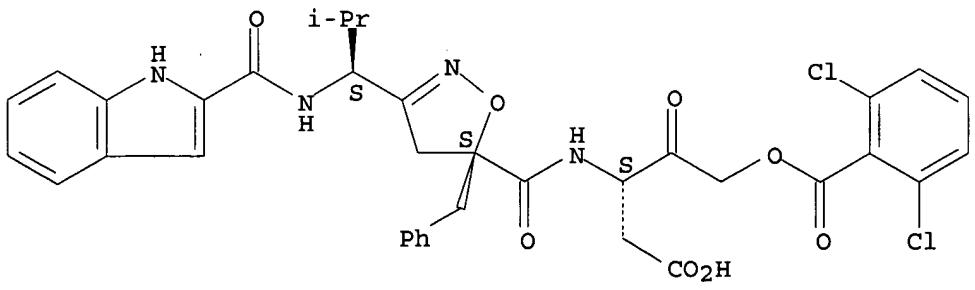
AB The present invention relates to isoxazoline derivs. I (R1 = alkyl, cycloalkyl, aryl, aralkyl, amino acid sidechain, (CH2)nCOOZ and n = 1,2 and Z = H, alkyl, aryl, cycloalkyl; R2 = H, alkyl, cycloalkyl, aryl, aralkyl, amino acid sidechain, (CH2)nOmR7 and n = 0,1,2 and m= 0,1 and R7 = alkyl, cycloalkyl, aryl, aralkyl, (CH2)nCOOR8 and n = 1,2 and R8 = alkyl, cycloalkyl, aralkyl; R3 = alkyl, cycloalkyl, aryl, aralkyl, amino acid sidechain; R4 = N-protected amino acid residue, COR9 and R9 = alkyl, etc., COLCOOR10 and L = linker and R10 = H, alkyl, etc.; R5,R6 = H, alkyl, cycloalkyl, aryl, aralkyl), the pharmaceutically acceptable salts, esters and stereochem. isomeric forms thereof, and the use of the deriv. in inhibiting the activity of caspases. The present invention also relates to a pharmaceutical compn. for preventing inflammation and apoptosis which comprises the isoxazoline deriv., pharmaceutically acceptable salts, esters and stereochem. isomeric forms thereof and the process for prepg. the same. The deriv. according to the present invention can be effectively used in treating diseases due to caspases, such as, for example the disease in which cells are abnormally died, dementia, cerebral stroke, AIDS, **diabetes**, gastric ulcer, hepatic injure by hepatitis, sepsis, organ transplantation rejection reaction and anti-inflammation.

IT **332020-92-5P 332020-94-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(isoxazoline deriv. caspase inhibitors for pharmaceutical uses)

RN 332020-92-5 HCAPLUS

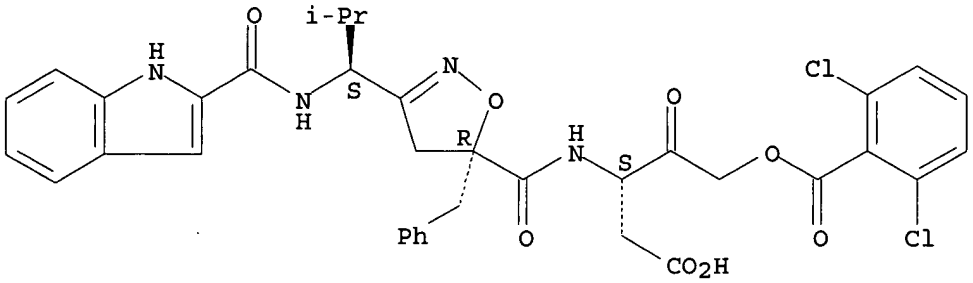
CN Benzoic acid, 2,6-dichloro-, (3S)-4-carboxy-3-[[[(5S)-4,5-dihydro-3-[(1S)-1-[(1H-indol-2-ylcarbonyl)amino]-2-methylpropyl]-5-(phenylmethyl)-5-isoxazolyl]carbonyl]amino]-2-oxobutyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 332020-94-7 HCAPLUS
CN Benzoic acid, 2,6-dichloro-, (3S)-4-carboxy-3-[[[(5R)-4,5-dihydro-3-[(1S)-1-[(1H-indol-2-ylcarbonyl)amino]-2-methylpropyl]-5-(phenylmethyl)-5-isoxazolyl]carbonyl]amino]-2-oxobutyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:227614 HCAPLUS
DOCUMENT NUMBER: 135:55802
TITLE: Pharmacology of caspase inhibitors in rabbit **cardiomyocytes** subjected to metabolic inhibition and recovery
AUTHOR(S): Li, Hai Ling; Karwatowska-Prokopczuk, Ewa; Mutomba, Martha; Wu, Joe; Karanewsky, Don; Valentino, Karen; Engler, Robert L.; Gottlieb, Roberta A.
CORPORATE SOURCE: Department of Veterans Affairs Medical Center, Research Service and Department of Medicine, San Diego, CA, 92161, USA
SOURCE: Antioxidants & Redox Signaling (2001), 3(1), 113-123
CODEN: ARSIF2; ISSN: 1523-0864
PUBLISHER: Mary Ann Liebert
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Protection of ischemic **myocardium** is an important unmet need in **reperfusion** therapy of acute **myocardial** infarction. **Myocardial ischemia** and **reperfusion** induce necrosis and apoptosis in **cardiomyocytes**. Caspase processing and activation are crit. steps in most receptor and nonreceptor pathways of apoptosis. Caspase inhibitors have been shown to reduce ischemia **reperfusion** injury in cardiac muscle. Information about dose response and time of administration are needed to optimize the design of preclin. studies. The authors used isolated adult rabbit **cardiomyocytes** subjected to metabolic inhibition (MI) and recovery to examine the role of caspases and caspase inhibitors, the dose response, and the timing of administration. In vitro inhibitory concns. (Ki) were detd. for purified caspases. **Cardiomyocytes** subjected to MI were treated with peptidomimetic fluoromethyl ketone inhibitors of caspases before or during MI, or at recovery. Caspase inhibitors were most effective when added before MI and included throughout recovery, but were partially protective if added after MI. The optimal concn. of the inhibitors tested was .apprx.10 .mu.M. Protection was sustained when cells were allowed to recover for 4 or 24 h. These results suggest that caspase activation is an important component of myocyte injury mediated by

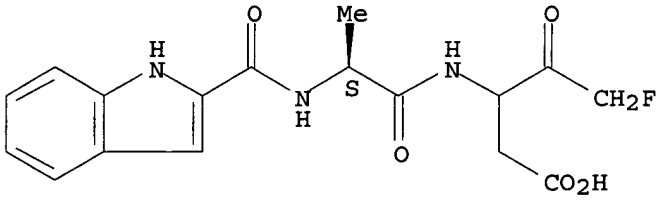
MI and recovery. Low doses of caspase inhibitors were identified that reduce injury in this model system, and further investigations using in vivo models are warranted.

IT **231950-93-9**, IDN 1529
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. of caspase inhibitors in rabbit cardiomyocytes subjected to metabolic inhibition and recovery in relation to treatment of heart ischemia reperfusion injury)

RN 231950-93-9 HCAPLUS

CN Pentanoic acid, 5-fluoro-3-[[(2S)-2-[(1H-indol-2-ylcarbonyl)amino]-1-oxopropyl]amino]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

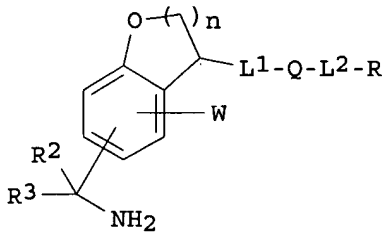
L31 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:152665 HCAPLUS
DOCUMENT NUMBER: 134:207826
TITLE: Preparation of substituted (aminoiminomethyl or aminomethyl)dihydrobenzofurans and benzopyrans as factor Xa and factor IIa inhibitors
INVENTOR(S): Burns, Christopher J.; Dankulich, William P.; McGarry, Daniel G.; Volz, Francis A.
PATENT ASSIGNEE(S): Aventis Pharmaceuticals Products Inc., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014358	A2	20010301	WO 2000-IB1562	20000812
WO 2001014358	A3	20010517		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1222182	A2	20020717	EP 2000-968181	20000812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 1999-150767P P 19990826
GB 1999-24155 A 19991012
WO 2000-IB1562 W 20000812

OTHER SOURCE(S): MARPAT 134:207826

GI



AB The title compds. [I; n = 1 or 2; W is H or a ring system substituent; R is hydrogen, cyano, cycloalkyl, cycloalkenyl, heterocyclyl,fused arylcycloalkyl, fused heteroarylcycloalkyl, etc.; R1 is hydrogen, alkyl, aralkyl, heteroaralkyl, acyl, aroyl, heteroaroyl, alkoxycarbonyl, aryloxycarbonyl or heteroaryloxycarbonyl; R2 and R3 are each hydrogen, or, taken together are :NR4; R4 is hydrogen, R5O2C, HO, cyano, R5CO, HCO, lower alkyl, nitro, etc.; R5 is alkyl, aryl, heteroaryl, aralkyl, or heteroaralkyl; L1 is alkylene, alkenylene or alkynylene; L2 is absent, alkylene, alkenylene, alkynylene, alkylene-O, alkenylene-O, etc., provided that when L2 is absent, then R is not hydrogen, and Q is attached to R through a carbon atom thereof; Q is NR8', O, CO, CO2, O2C, NR8'(X1), C(X)NR8', NR8C(X1)O, etc.; provided that a nitrogen atom or oxygen atom of Q is not directly bonded to a carbon atom of L1 or L2 having a double bond or triple bond, or Q-L2-R is cycloalkyl, cycloalkenyl, heterocyclyl, fused arylcycloalkyl, fused heteroarylcycloalkyl, etc., provided that a nitrogen atom or oxygen atom of Q is not directly bonded to a carbon atom of L1 having a double bond or triple bond; X1 is O or S; R8' is hydrogen, alkyl, aralkyl, heteroaralkyl, acyl, aroyl, heteroaroyl or alkoxycarbonyl; R8 is hydrogen, alkyl, aralkyl, heteroaralkyl, acyl, aroyl or heteroaroyl; and m is 0, 1 or 2], oxides thereof, pharmaceutically acceptable salts, solvates thereof, or prodrugs thereof are prepd. These compds. inhibit the formation of simultaneously directly inhibiting both Factor Xa and Factor IIa (thrombin) and are useful for treating pathol. conditions in a patient that may be ameliorated by administration of such compds. The pathol. conditions include venous vasculature, arterial vasculature, abnormal thrombus formation, acute **myocardial** infarction, unstable angina, thromboembolism, acute vessel closure assocd. with thrombolytic therapy, percutaneous transluminal coronary angioplasty, transient ischemic attacks, stroke, intermittent claudication or bypass grafting of the coronary or peripheral arteries, vessel luminal narrowing, restenosis post coronary or venous angioplasty, maintenance of vascular access patency in longterm hemodialysis patients, pathol. thrombus formation occurring in the veins of the lower extremities following abdominal, knee and hip surgery, a risk of pulmonary thromboembolism, or disseminated systemic intravascular coagulopathy occurring in vascular systems during septic shock, certain viral infections or cancer (no data). Thus, To a cooled (0.degree.) soln. of 5-(pyrid-2-yl)thiophene-2-carboxylic acid and 4-methylmorpholine in CH2Cl2 is added dropwise a soln. of iso-Pr chloroformate in toluene, stirred 30 min, treated with 2-[5-(N-tert-butoxycarbonyl)carbamimidoyl-2,3-dihydrobenzofuran-3-

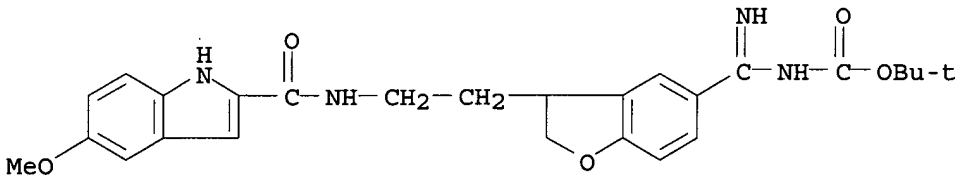
yl]ethylamine in DMF, and the reaction mixt. was allowed to warm to room temp. overnight to give 5-pyridin-2-ylthiophene-2-carboxylic acid [2-[5-(N-tert-butoxycarbonyl)carbamimidoyl-2,3-dihydrobenzofuran-3-yl]ethyl]amide which was stirred with H2O and CF3CO2H in CH2Cl2 for 3 h to give 5-(pyridin-2-yl)thiophene-2-carboxylic acid [2-(5-carbamimidoyl-2,3-dihydrobenzofuran-3-yl)ethyl]amide.

IT **328124-89-6P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of substituted (aminoiminomethyl or aminomethyl)dihydrobenzofurans and -benzopyrans as inhibitors of factor Xa and factor IIa)

RN 328124-89-6 HCAPLUS

CN Carbamic acid, [[2,3-dihydro-3-[2-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]ethyl]-5-benzofuranyl]iminomethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

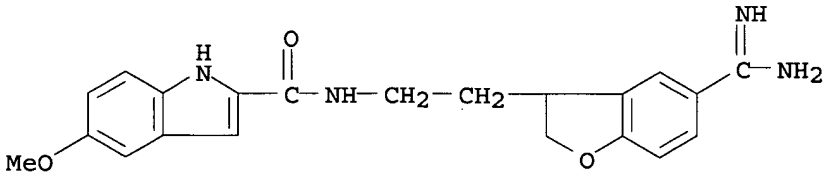


IT **328124-08-9P 328124-37-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted (aminoiminomethyl or aminomethyl)dihydrobenzofurans and -benzopyrans as inhibitors of factor Xa and factor IIa)

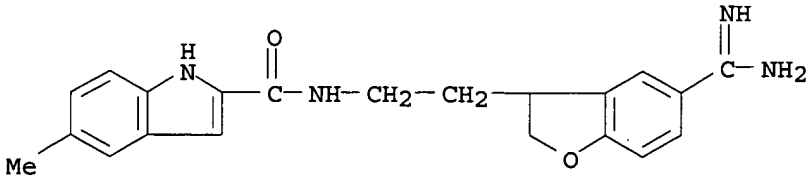
RN 328124-08-9 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[5-(aminoiminomethyl)-2,3-dihydro-3-benzofuranyl]ethyl]-5-methoxy- (9CI) (CA INDEX NAME)

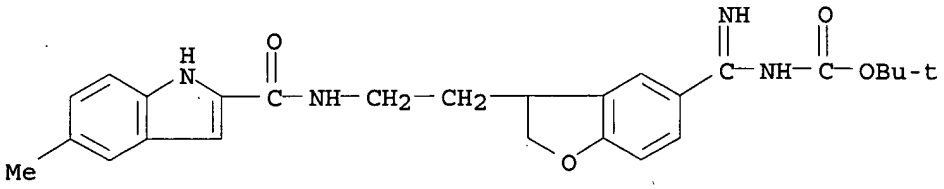


RN 328124-37-4 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[5-(aminoiminomethyl)-2,3-dihydro-3-benzofuranyl]ethyl]-5-methyl- (9CI) (CA INDEX NAME)



IT **328124-64-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of substituted (aminoiminomethyl or aminomethyl)dihydrobenzofurans and -benzopyrans as inhibitors of factor Xa and factor IIa)
RN 328124-64-7 HCAPLUS
CN Carbamic acid, [[2,3-dihydro-3-[2-[[(5-methyl-1H-indol-2-yl)carbonyl]amino]ethyl]-5-benzofuranyl]iminomethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L31 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:573516 HCAPLUS
DOCUMENT NUMBER: 133:168404
TITLE: Osmotic system for delivery of solid amorphous dispersions of drugs
INVENTOR(S): Appel, Leah Elizabeth; Curatolo, William John; Herbig, Scott Max; Nightingale, James Alan Schriver; Thombre, Avinash Govind
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

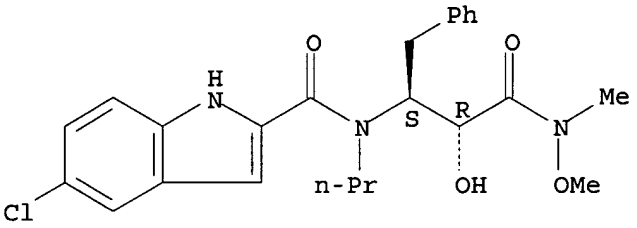
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1027888	A2	20000816	EP 2000-300572	20000126
EP 1027888	A3	20010228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000229846	A2	20000822	JP 2000-33132	20000210
BR 2000000358	A	20010821	BR 2000-358	20000210

PRIORITY APPLN. INFO.: US 1999-119406P P 19990210
AB Controlled release dosage forms for low soly. drugs comprise an amorphous solid dispersion of the drug coated with a non-dissolving and non-eroding coating that controls the influx of water to the core so as to cause extrusion of a portion of the core, as well as a method of treating a disease or disorder comprising administering such dosage form to a person. A solid dispersion was prepd. from [R-(R*,S*)]-5-chloro-N-[2-hydroxy-3-[methoxymethylamino-3-oxo-1-(phenylmethyl)propyl]propyl]-1H-indole-2-carboxamide (a **glycogen phosphorylase inhibitor**) and hydroxypropyl Me cellulose acetate succinate.
IT **9035-74-9**, Glycogen phosphorylase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; osmotic system for delivery of solid amorphous dispersions of drugs)

RN 9035-74-9 HCAPLUS
CN Phosphorylase (9CI) (CA INDEX NAME)

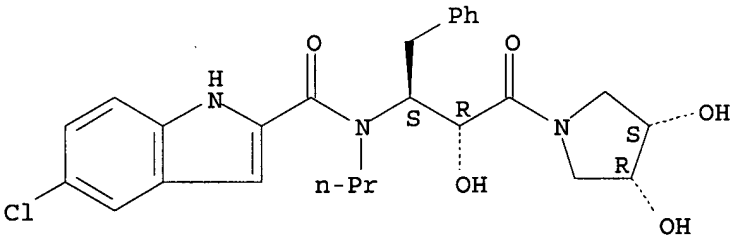
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **288154-34-7 288154-35-8**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(osmotic system for delivery of solid amorphous dispersions of drugs)
RN 288154-34-7 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]-N-propyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 288154-35-8 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-N-propyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:260225 HCAPLUS
DOCUMENT NUMBER: 132:294010
TITLE: Preparation of diaminopropionic acid derivatives as intracellular adhesion molecule-1 (ICAM-1) binding inhibitors
INVENTOR(S): Fotouhi, Nader; Gillespie, Paul; Guthrie, Robert William; Pietranico-Cole, Sherrie Lynn; Yun, Weiya
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 259 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000021920	A1	20000420	WO 1999-EP7620	19991012	
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6331640	B1	20011218	US 1999-407534	19990929	
BR 9914602	A	20010703	BR 1999-14602	19991012	
EP 1121342	A1	20010808	EP 1999-953772	19991012	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002527416	T2	20020827	JP 2000-575829	19991012	
US 2002052512	A1	20020502	US 2001-879700	20010612	

PRIORITY APPLN. INFO.: US 1998-104120P P 19981013
US 1999-407534 A3 19990929
WO 1999-EP7620 W 19991012

OTHER SOURCE(S): MARPAT 132:294010

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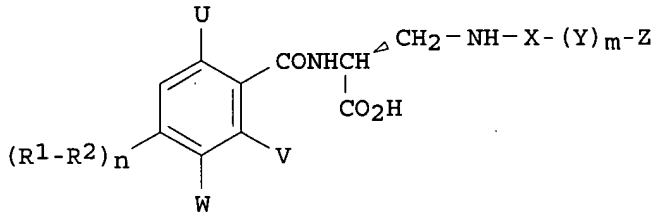

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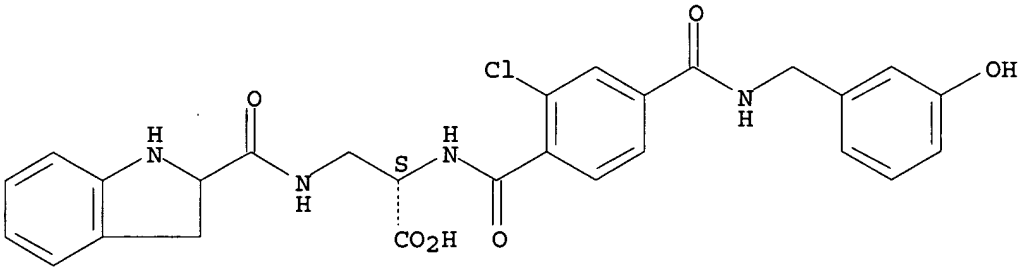
AB Diaminopropionic acid derivs. I [R1 = substituted 1-naphthyl, 4-indolyl, 4-benzimidazolyl, 4-benzodiazolyl, 4-benzotriazolyl, or phenyl; R2 = CHR3NHCO (R3 = H, carboxy, alkyl), CH2CH2CO, 1,2-cyclopropanediylcarbonyl, OCH2CO, CH:CHCHR3, CH2CH2CH(OH), CONHCHR3, or CH2NH-5,1-tetrazolediyl; U, V, W = H, halo, alkyl provided that U and V are not both hydrogen; X = CO, phenylalkylene, sulfonyl; Y = alkylene which may be substituted by amino or cycloalkyl, alkenylene, alkylenethio; Z = H, alkylthio, CO2H, CONH2, 1-adamantyl, diphenylmethyl, 3-[[(5-chloro-2-pyridinyl)amino]carbonyl]-2-pyrazinyl, hydroxy, phenylmethoxy, 2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]phenyl, [(2,6-dichlorophenyl)methoxy], Ph, (un)substituted cycloalkyl or aryl or fused ring system which may contain 0-3 heteroatoms; m, n = 0, 1] or their pharmaceutically acceptable salts or esters were prepd. and are useful for treating rheumatoid arthritis, psoriasis, multiple sclerosis, Crohn's disease, ulcerative colitis, atherosclerosis, restenosis, pancreatitis, transplant rejection, delayed graft function and diseases of **ischemia reperfusion** injury, including acute **myocardial** infarction and stroke. Thus, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-(3-methoxybenzoylamino)-L-alanine was prepd. by the solid-phase method and showed IC50 = 1.2 nM in the LFA-1 (lymphocyte function-assocd. antigen-1)/ICAM-1 protein-protein assay.

IT **264275-03-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of diaminopropionic acid derivs. as intracellular adhesion mol.-1 (ICAM-1) binding inhibitors)
RN 264275-03-8 HCAPLUS
CN L-Alanine, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-[[(2,3-dihydro-1H-indol-2-yl)carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:98049 HCAPLUS
DOCUMENT NUMBER: 132:148495
TITLE: Preparation of **inhibitors** of human **glycogen phosphorylase** and their therapeutical applications
INVENTOR(S): Rath, Virginia Leigh; Hoover, Dennis Jay; Ammirati, Mark
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 42 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 978279	A1	20000209	EP 1999-306047	19990729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002031816	A1	20020314	US 1999-369214	19990805
JP 2000083662	A2	20000328	JP 1999-225128	19990809
BR 9903571	A	20010306	BR 1999-3571	19990809

PRIORITY APPLN. INFO.: US 1998-95790P P 19980807
OTHER SOURCE(S): MARPAT 132:148495
AB The present invention is directed to a novel binding site for a **glycogen phosphorylase inhibitor** found within a **glycogen phosphorylase** enzyme. The novel binding site allows the design of novel **glycogen phosphorylase inhibitors**. A method of treatment of hyperglycemia, hyperinsulinemia, hyperlipidemia, insulin resistance or tissue ischemia using the **glycogen phosphorylase inhibitor**

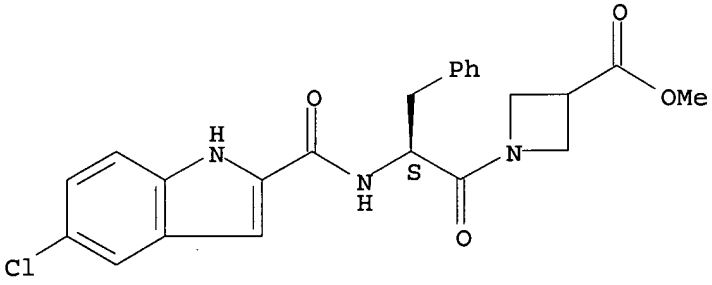
is disclosed.

IT **257624-03-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of inhibitors of human glycogen phosphorylase and their therapeutical applications)

RN 257624-03-6 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[(2S)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-1-oxo-3-phenylpropyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

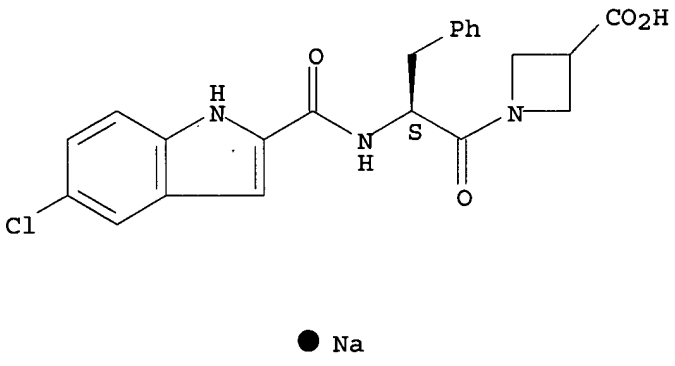


IT **257624-04-7P 257624-05-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of inhibitors of human glycogen phosphorylase and their therapeutical applications)

RN 257624-04-7 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[(2S)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-1-oxo-3-phenylpropyl]-, monosodium salt (9CI) (CA INDEX NAME)

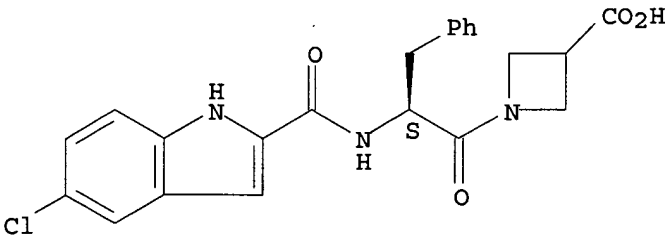
Absolute stereochemistry.



RN 257624-05-8 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[(2S)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-1-oxo-3-phenylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



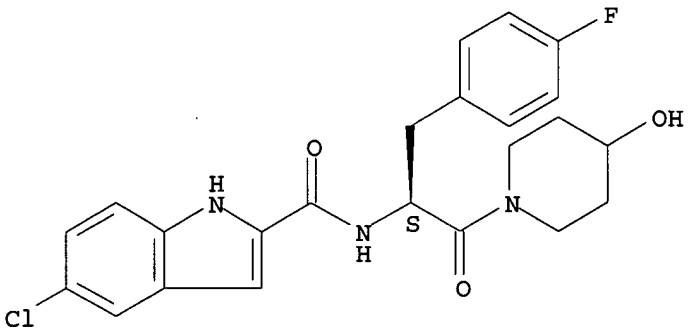
IT **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(prepn. of **inhibitors** of human glycogen phosphorylase and their therapeutical applications)
RN 9035-74-9 HCAPLUS
CN Phosphorylase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **9035-74-9D**, Phosphorylase, **inhibitor** complexes
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(prepn. of **inhibitors** of human glycogen phosphorylase and their therapeutical applications)
RN 9035-74-9 HCAPLUS
CN Phosphorylase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:15754 HCAPLUS
DOCUMENT NUMBER: 132:288599
TITLE: Pharmacological interference with hepatic glucose production
AUTHOR(S): Burger, H.-J.; Schubert, G.; Hemmerle, H.; Kramer, W.; Herling, A. W.
CORPORATE SOURCE: Hoechst Marion Roussel Deutschland GmbH, Frankfurt am Main, 65926, Germany
SOURCE: Annals of the New York Academy of Sciences (1999), 892(Metabolic Syndrome X), 312-314
CODEN: ANYAA9; ISSN: 0077-8923
PUBLISHER: New York Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study was designed to characterize different pharmacol. approaches to interfere with hepatic glucose prodn. It can be concluded that the best way to reduce hepatic glucose prodn. is the inhibition of hepatic glucose-6- phosphatase activity. Pharmacol. approaches to reduce hepatic glucose prodn. are rational objectives for type 2 **diabetes** therapy.
IT **186430-23-9**, CP 320626
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacol. interference with hepatic glucose prodn.)
RN 186430-23-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

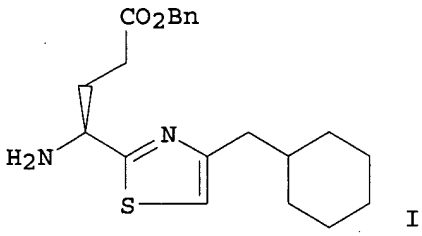


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:613914 HCAPLUS
DOCUMENT NUMBER: 131:257875
TITLE: Preparation of heterocyclyl phosphotyrosine derivatives as SH2-mediated signal transduction inhibitors
INVENTOR(S): Buchanan, John; Bohacek, Regine; Vu, Chi B.; Luke, George P.
PATENT ASSIGNEE(S): Ariad Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 194 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947529	A1	19990923	WO 1999-US5970	19990318
W: CA, CZ, JP, MX, RU, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2319493	AA	19990923	CA 1999-2319493	19990318
EP 1064289	A1	20010103	EP 1999-912685	19990318
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002506873	T2	20020305	JP 2000-536724	19990318

PRIORITY APPLN. INFO.: US 1998-78412P P 19980318
US 1998-108084P P 19981112
WO 1999-US5970 W 19990318
OTHER SOURCE(S): MARPAT 131:257875
GI



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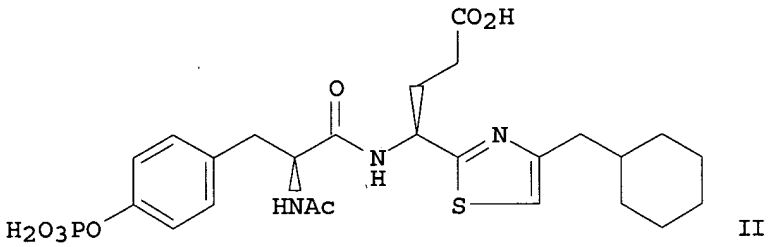


II

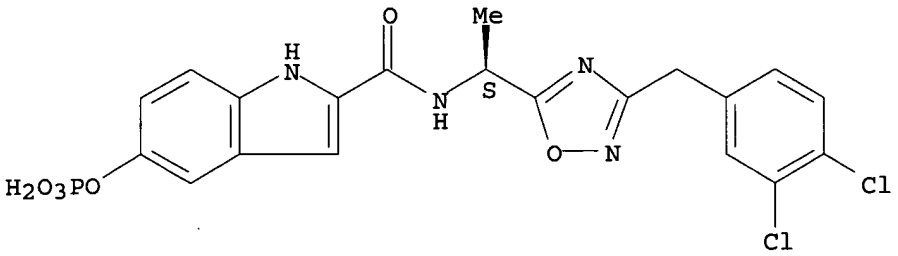
AB Heterocyclic phosphotyrosine derivs. were prepd. for inhibiting intracellular signal transduction, esp. intracellular signal transduction mediated by a PDGF receptor protein, EGF receptor protein, HER2/Neu receptor protein, fibroblast growth factor receptor protein, focal adhesion kinase protein, p130 protein, or p68 protein. For example, BOC-Tyr(PO3Bn2)-OH (BOC = tert-butoxycarbonyl; Bn = benzyl) and the thiazolylamine salt (I).cntdot.TFA (four step prepn. given) were coupled, the phosphate deprotected, the amine acylated, and the carboxylic acid deprotected to form the title compd. (II). In an assay for binding affinities to Src SH2, thirteen compds. of the invention were detd. to have IC50 values of < 50.mu.M. In an assay for binding affinities to Zap-70 SH2, fourteen compds. of the invention exhibited IC50 values of < 50.mu.M. This invention also relates to pharmaceutical compns. contg. the compds. and prophylactic and therapeutic methods involving pharmaceutical and veterinary administration of the compds. for proliferative disease, cancer, restenosis, osteoporosis, inflammation, allergies, **cardiovascular** disease, or immunosuppression.

IT **244210-62-6P**
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of heterocyclyl phosphotyrosine derivs. as SH2-mediated signal transduction inhibitors)

RN 244210-62-6 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[(1S)-1-[3-[(3,4-dichlorophenyl)methyl]-1,2,4-oxadiazol-5-yl]ethyl]-5-(phosphonooxy)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:354425 HCAPLUS
DOCUMENT NUMBER: 131:9635
TITLE: Combination of an aldose reductase **inhibitor** and a **glycogen phosphorylase inhibitor**
INVENTOR(S): Mylari, Banavara Lakshman; Hoover, Dennis Jay; Hulin, Bernard; Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926659	A1	19990603	WO 1998-IB1752	19981102
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2310069	AA	19990603	CA 1998-2310069	19981102
AU 9895558	A1	19990615	AU 1998-95558	19981102
AU 733304	B2	20010510		
EP 1032424	A1	20000906	EP 1998-949193	19981102
EP 1032424	B1	20010912		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9814698	A	20001003	BR 1998-14698	19981102
AT 205403	E	20010915	AT 1998-949193	19981102
ES 2161548	T3	20011201	ES 1998-949193	19981102
JP 2002504478	T2	20020212	JP 2000-521860	19981102
ZA 9810636	A	20000522	ZA 1998-10636	19981120
NO 2000002164	A	20000719	NO 2000-2164	20000427

PRIORITY APPLN. INFO.: US 1997-66365P P 19971121
WO 1998-IB1752 W 19981102

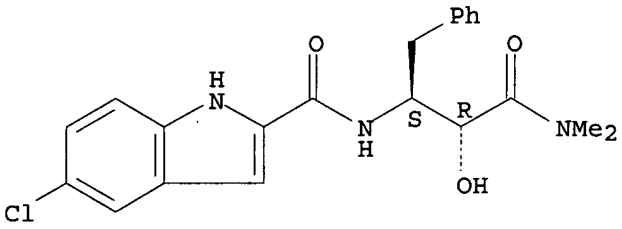
AB Pharmaceutical compns., kits and methods comprising combination of aldose reductase inhibitors (0.1-20 mg/kg) and **glycogen phosphorylase inhibitors** (0.1-15 mg/kg), useful for treatment of insulin resistant conditions such as **diabetes**,

hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis, and tissue ischemia, etc., are described. E.g., a tablet formulation contained an active ingredient (an aldose reductase **inhibitor**, a **glycogen phosphorylase inhibitor**, or a combination of the two) 0.25-100, starch 45, microcryst. cellulose 35, PVP (as 10% soln. in water) 4, Na CM-cellulose 4.5, Mg stearate 0.5, and talc 1 mg/tablet, resp.

IT **186392-40-5 186392-43-8 186392-49-4**
186392-53-0 186392-64-3 186429-64-1
186429-78-7 186430-11-5 186430-23-9
186430-41-1 186430-52-4 186431-27-6
208830-24-4 208830-25-5 225929-30-6
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

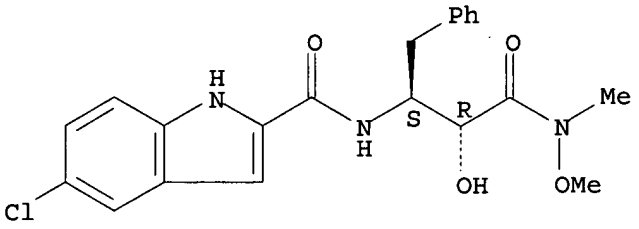
RN 186392-40-5 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



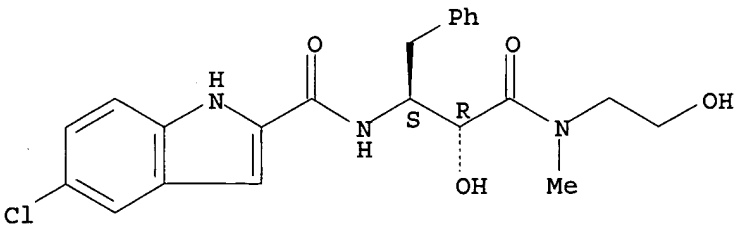
RN 186392-43-8 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



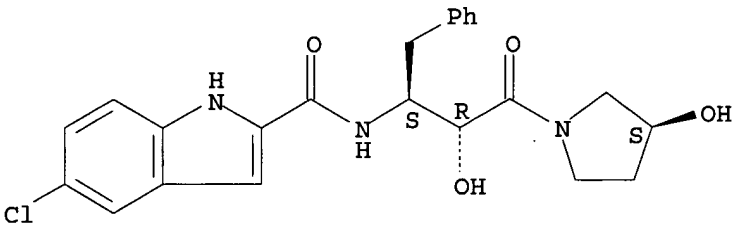
RN 186392-49-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(2-hydroxyethyl)methylamino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



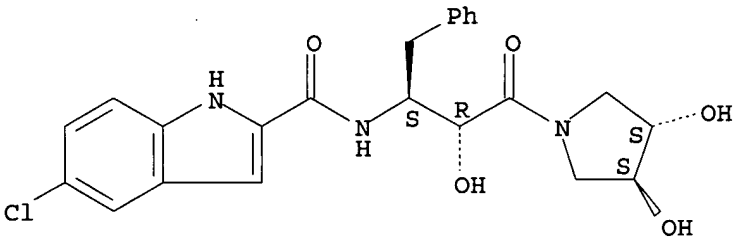
RN 186392-53-0 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(3S)-3-hydroxy-1-pyrrolidinyl]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



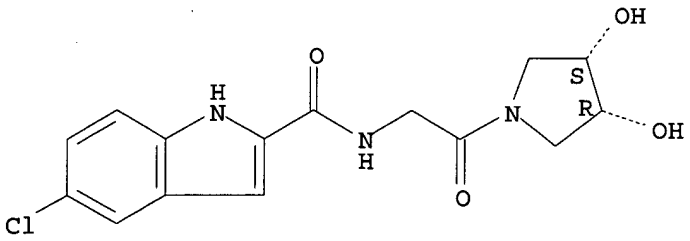
RN 186392-64-3 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



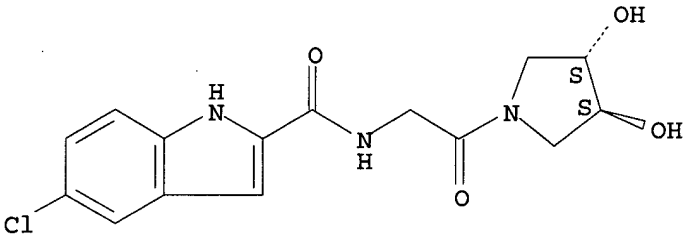
RN 186429-64-1 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxoethyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



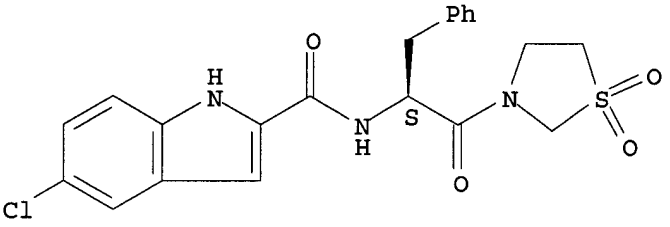
RN 186429-78-7 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



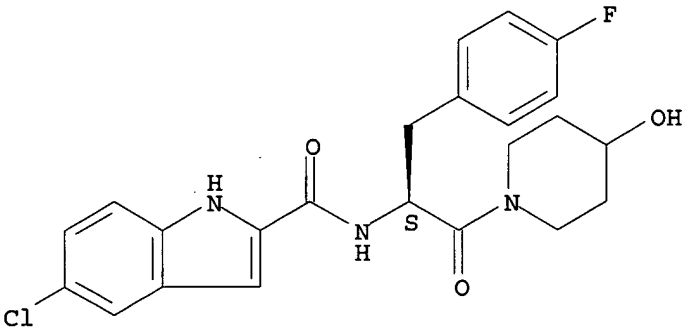
RN 186430-11-5 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(1,1-dioxido-3-thiazolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



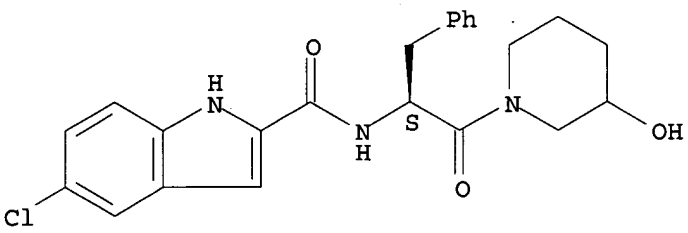
RN 186430-23-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



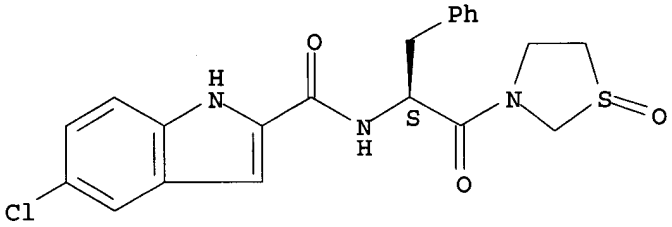
RN 186430-41-1 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-piperidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



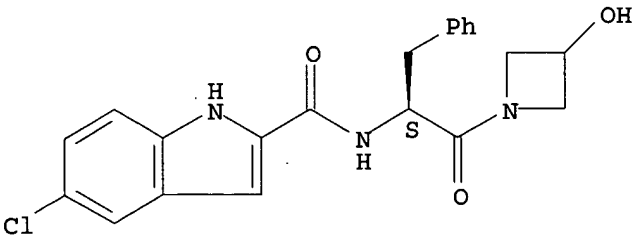
RN 186430-52-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(1-oxido-3-thiazolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



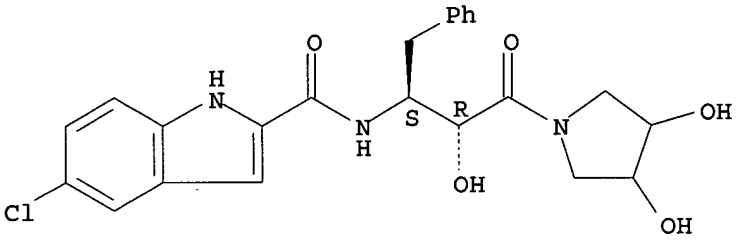
RN 186431-27-6 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-azetidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



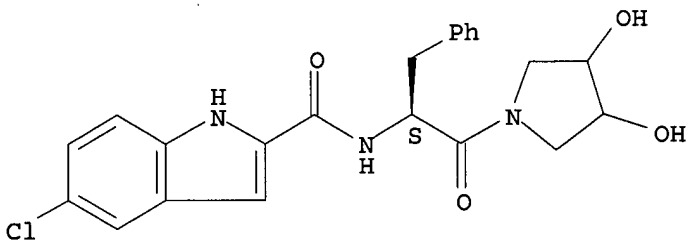
RN 208830-24-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(3,4-dihydroxy-1-pyrrolidinyl)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



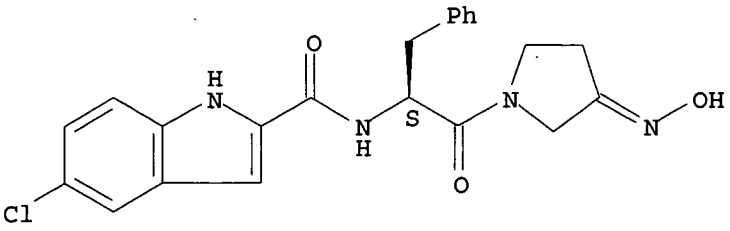
RN 208830-25-5 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3,4-dihydroxy-1-pyrrolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 225929-30-6 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[3-(hydroxyimino)-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

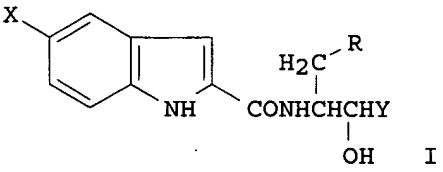
Absolute stereochemistry.
Double bond geometry unknown.



IT **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(compns. for **inhibitors** of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)
RN 9035-74-9 HCAPLUS
CN Phosphorylase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:450920 HCAPLUS
DOCUMENT NUMBER: 129:189205
TITLE: Indole-2-carboxamide **inhibitors** of human liver **glycogen phosphorylase**
AUTHOR(S): Hoover, Dennis J.; Lefkowitz-Snow, Sheri; Burgess-Henry, Jana L.; Martin, William H.; Armento, Sandra J.; Stock, Ingrid A.; McPherson, R. Kirk; Genereux, Paul E.; Gibbs, E. Michael; Treadway, Judith L.
CORPORATE SOURCE: Department of Cardiovascular and Metabolic Diseases Medicinal Chemistry, Central Research Division, Pfizer Inc., Groton, CT, 06340, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(16), 2934-2938
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



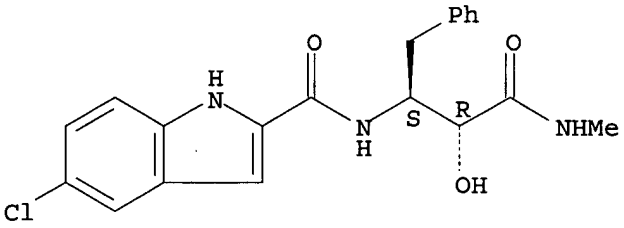
AB Indole-2-carboxamide derivs. (I; X = Cl, F, Br, H, OMe; R = Ph, cyclohexyl, H, F; Y = CONMe2, CONHMe, CO2Me, CO2H, CH2OH, CONH2, etc.) were prepd. I are potent **inhibitors** of human liver

glycogen phosphorylase which are active in cells, and produce hypoglycemic activity on oral administration in a rodent model of type 2 **diabetes**. I [CP-320626; X = Cl, R = F, Y = CO(1-piperidin-4-ol)] produced oral activity at 10 mg/kg.

IT **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(human liver; indole-2-carboxamide **inhibitors** of human liver glycogen phosphorylase)
RN 9035-74-9 HCAPLUS
CN Phosphorylase (9CI) (CA INDEX NAME)

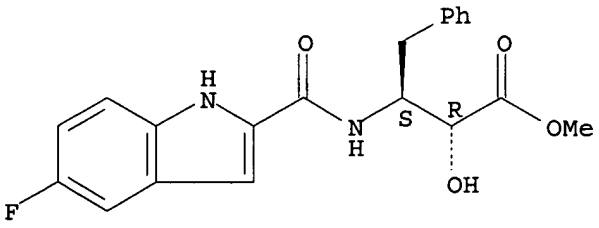
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
IT **186392-10-9P 186392-11-0P 186392-12-1P**
186392-13-2P 186392-22-3P 186392-32-5P
186392-33-6P 186392-34-7P 186392-38-1P
186392-40-5P 186392-56-3P 186429-59-4P
186429-60-7P 186430-05-7P 186430-23-9P
186430-32-0P 186430-34-2P 186430-36-4P
186430-37-5P 186430-39-7P 186430-44-4P
186432-25-7P 186432-26-8P 211677-10-0P
211677-11-1P 211677-12-2P 211677-13-3P
211677-14-4P 211677-15-5P 211677-16-6P
211677-17-7P 211677-18-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indole-2-carboxamide inhibitors of human liver glycogen phosphorylase)
RN 186392-10-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



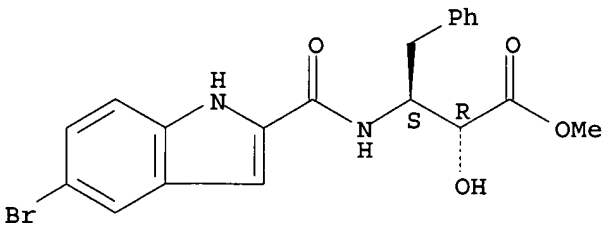
RN 186392-11-0 HCAPLUS
CN Benzenebutanoic acid, .beta.-[[(5-fluoro-1H-indol-2-yl)carbonyl]amino]-.alpha.-hydroxy-, methyl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



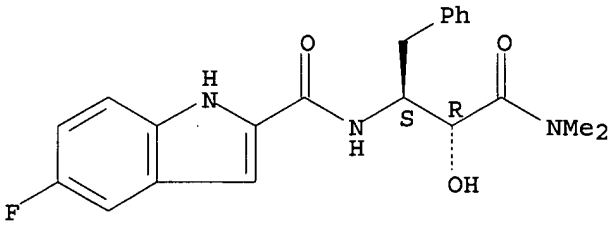
RN 186392-12-1 HCAPLUS
CN Benzenebutanoic acid, .beta.-[[(5-bromo-1H-indol-2-yl)carbonyl]amino]-.alpha.-hydroxy-, methyl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



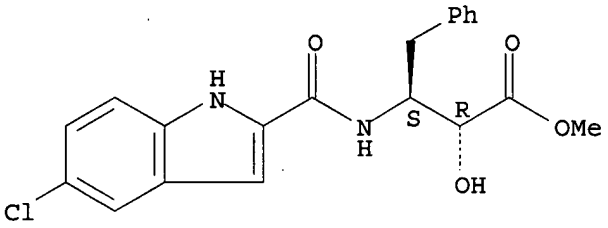
RN 186392-13-2 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



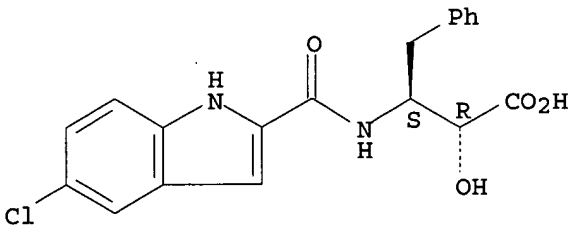
RN 186392-22-3 HCAPLUS
CN Benzenebutanoic acid, .beta.-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-.alpha.-hydroxy-, methyl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



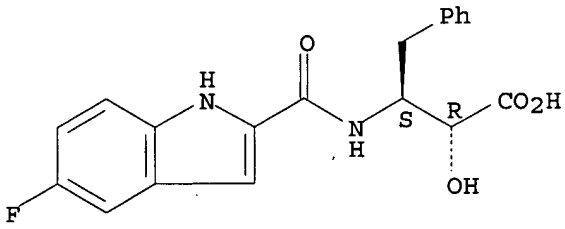
RN 186392-32-5 HCAPLUS
CN Benzenebutanoic acid, .beta.-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-.alpha.-hydroxy-, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



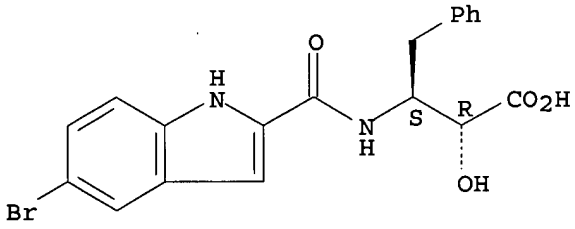
RN 186392-33-6 HCAPLUS
CN Benzenebutanoic acid, .beta.-[[(5-fluoro-1H-indol-2-yl)carbonyl]amino]-.alpha.-hydroxy-, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



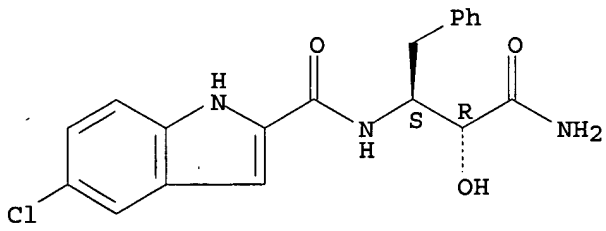
RN 186392-34-7 HCAPLUS
CN Benzenebutanoic acid, .beta.-[[(5-bromo-1H-indol-2-yl)carbonyl]amino]-.alpha.-hydroxy-, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186392-38-1 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-3-amino-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-5-chloro- (9CI) (CA INDEX NAME)

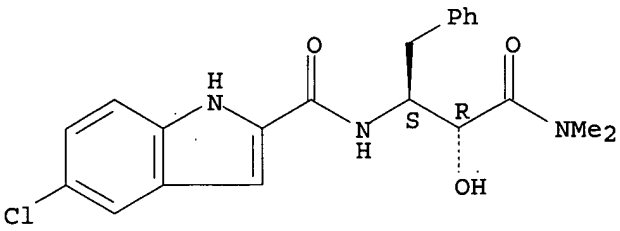
Absolute stereochemistry.



RN 186392-40-5 HCAPLUS

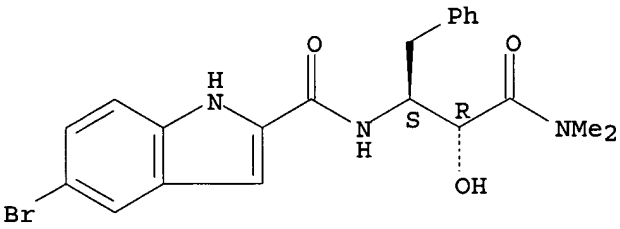
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



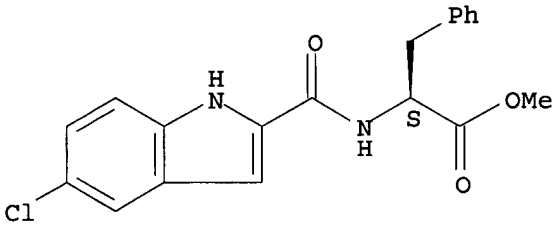
RN 186392-56-3 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-bromo-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



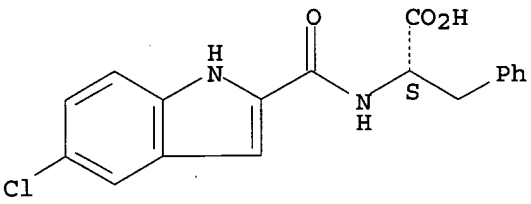
RN 186429-59-4 HCAPLUS
CN L-Phenylalanine, N-[(5-chloro-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



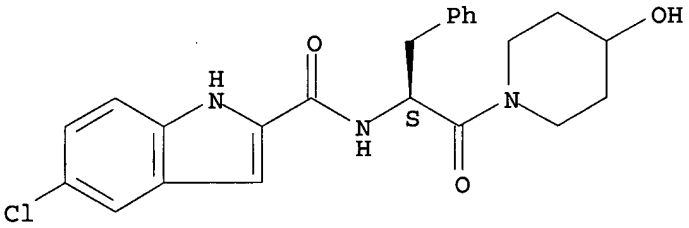
RN 186429-60-7 HCAPLUS
CN L-Phenylalanine, N-[(5-chloro-1H-indol-2-yl)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



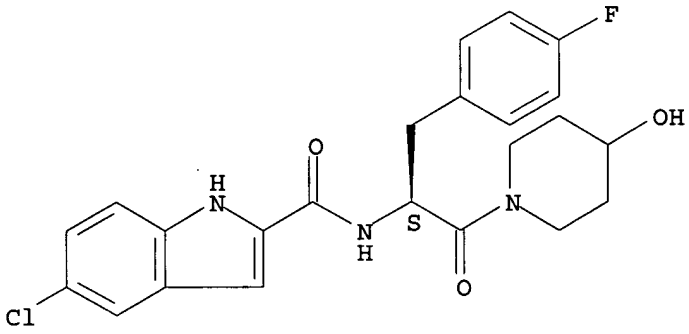
RN 186430-05-7 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(4-hydroxy-1-piperidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



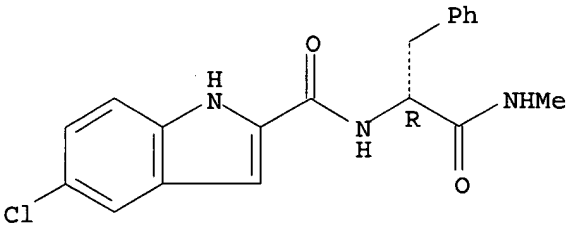
RN 186430-23-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



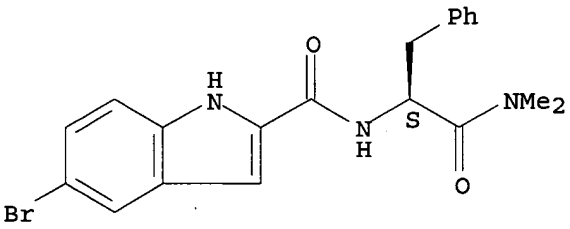
RN 186430-32-0 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R)-2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



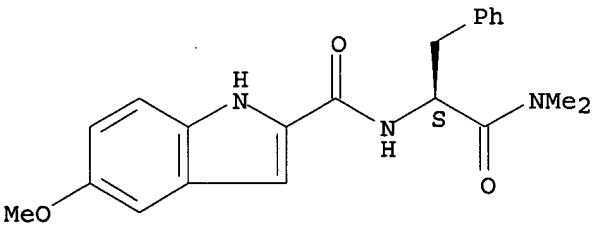
RN 186430-34-2 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-bromo-N-[(1S)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



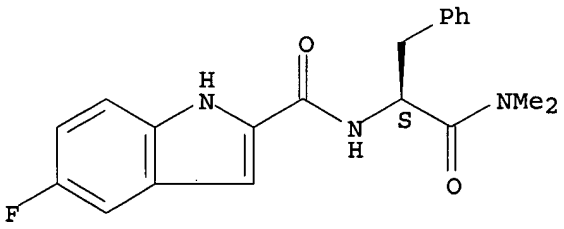
RN 186430-36-4 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]-5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186430-37-5 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]-5-fluoro- (9CI) (CA INDEX NAME)

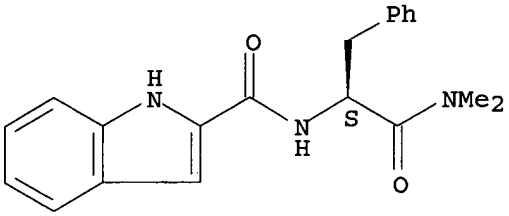
Absolute stereochemistry.



RN 186430-39-7 HCAPLUS

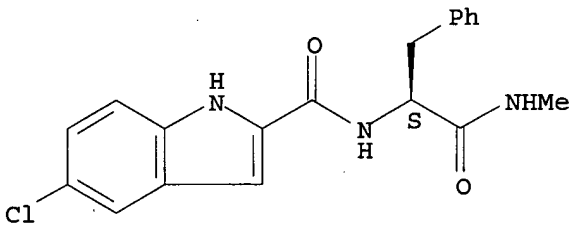
CN 1H-Indole-2-carboxamide, N-[(1S)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



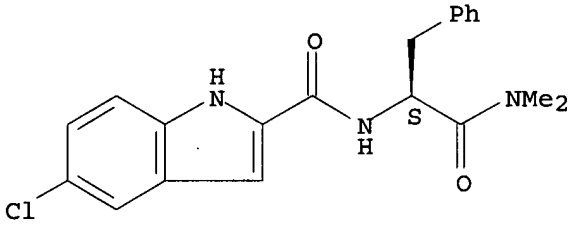
RN 186430-44-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



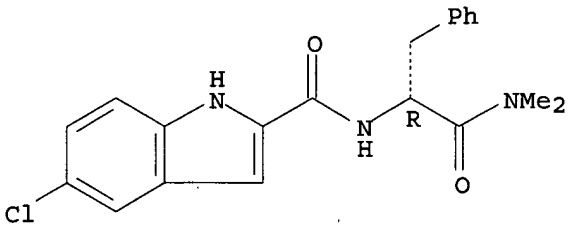
RN 186432-25-7 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



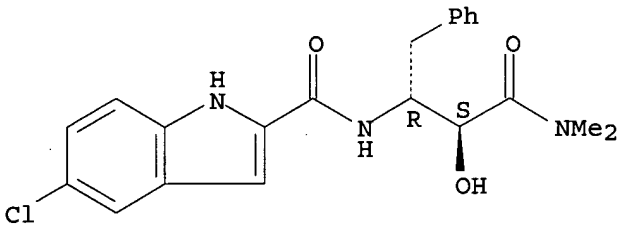
RN 186432-26-8 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



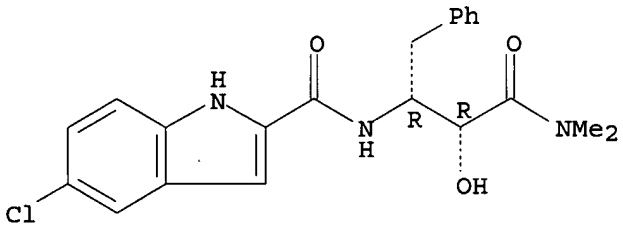
RN 211677-10-0 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2S)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



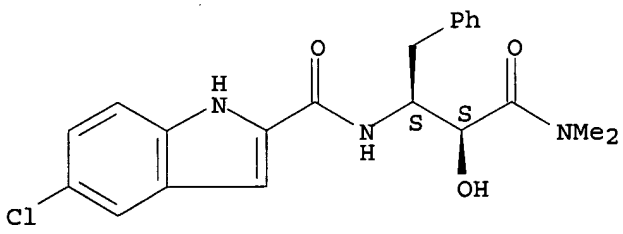
RN 211677-11-1 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 211677-12-2 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2S)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

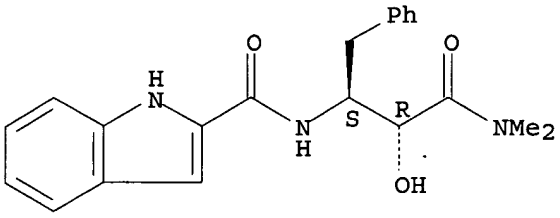
Absolute stereochemistry.



RN 211677-13-3 HCAPLUS

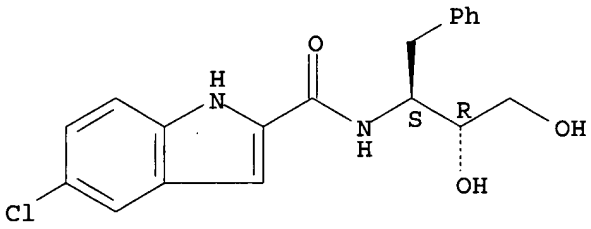
CN 1H-Indole-2-carboxamide, N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



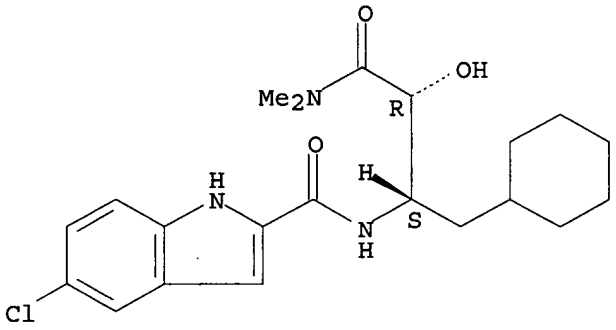
RN 211677-14-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2,3-dihydroxy-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



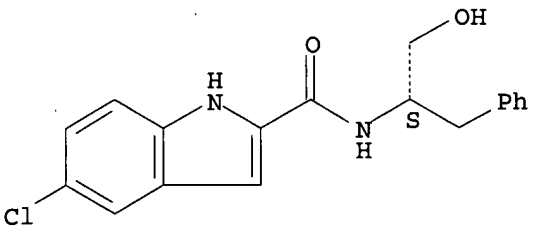
RN 211677-15-5 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-1-(cyclohexylmethyl)-3-(dimethylamino)-2-hydroxy-3-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



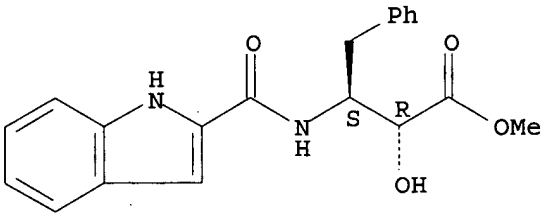
RN 211677-16-6 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-(hydroxymethyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



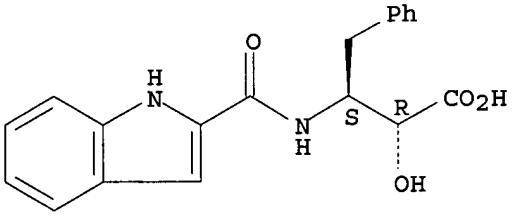
RN 211677-17-7 HCAPLUS
CN Benzenebutanoic acid, .alpha.-hydroxy-.beta.-[(1H-indol-2-ylcarbonyl)amino]-, methyl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 211677-18-8 HCAPLUS
CN Benzenebutanoic acid, .alpha.-hydroxy-.beta.-[(1H-indol-2-ylcarbonyl)amino]-, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

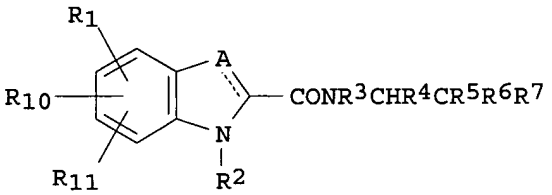
Absolute stereochemistry.



L31 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:388320 HCAPLUS
DOCUMENT NUMBER: 129:72196
TITLE: Use of **glycogen phosphorylase inhibitor** for reducing non-cardiac tissue damage resulting from ischemia
INVENTOR(S): Hoover, Dennis J.; Martin, William Holt; Tracey, Wayne Ross; Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 52 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 846464	A2	19980610	EP 1997-309727	19971203
EP 846464	A3	19990217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 5952322	A	19990914	US 1997-978384	19971125
CA 2223317	AA	19980605	CA 1997-2223317	19971203
JP 10194990	A2	19980728	JP 1997-332523	19971203
JP 3277147	B2	20020422		
AU 9746869	A1	19980611	AU 1997-46869	19971204
AU 717547	B2	20000330		
ZA 9710907	A	19990604	ZA 1997-10907	19971204

PRIORITY APPLN. INFO.: US 1996-31584P P 19961205
OTHER SOURCE(S): MARPAT 129:72196
GI



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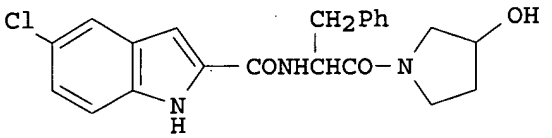


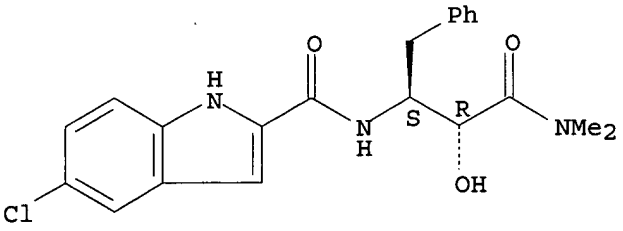
II

AB The use of a **glycogen phosphorylase inhibitor** for the manuf. of a medicament for reducing non-cardiac tissue damage resulting from ischemia or hypoxia. The tissue is brain, liver, kidney, lung, gut, skeletal muscle, spleen, pancreas, nerve, spinal code, retina tissue, the vasculature or intestinal tissue. Said **glycogen phosphorylase inhibitor** is represented by a compd. of formula [I; A = C(X): (wherein X = H, C1-4 alkyl, halo) when the dotted line is a bond; A = CH2 or CH(C1-4 alkyl) when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6-, or 7-NO2, cyano, C1-4 alkyl or alkoxy, CH2F, CF2H, CF3; R2 = H; R3 = H, C1-5 alkyl; R4 = H, Me, Et, n-Pr, C1-3 hydroxyalkyl, C1-3 alkoxy-C1-3 alkyl, phenyl-C1-4 alkyl, thien-2- or -3-yl-C1-4 alkyl, furan-2- or -3-yl-C1-4 alkyl, etc.; R5 = H, OH, F, C1-5 alkyl or alkoxy, C1-6 alkanoyl, amino-C1-4 alkoxy, mono-N- or di-N, N-C1-4 alkyl amino-C1-4 alkoxy, carboxy-C1-4 alkoxy, etc.; R7 = H, F, C1-5 alkyl; or R5 and R7 are taken together to form oxo; R6 = CO2H, C1-8 alkoxycarbonyl, (un)substituted CONH2, COR12; wherein R12 = piperazin-1-yl, 4-(C1-4 alkyl)piperazin-1-yl, 4-formylpiperazin-1-yl, morpholino, thiomorpholino, 1-oxothiomorpholino, 1,1-dioxothiomorpholino, thizolidin-3-yl, etc.], e.g. indolecarboxamide (II) which **inhibited** human liver **glycogen phosphorylase** a (HLGPa) and human muscle **glycogen** phosphorylase a (HMGPa) with IC50 of 45 and 85 nM, resp.

IT **186392-40-5 186392-43-8 186392-46-1**
186392-49-4 186392-53-0 186392-64-3
186429-66-3 186430-04-6 186430-23-9
186430-40-0 186431-27-6 186431-28-7
208830-24-4 208830-25-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

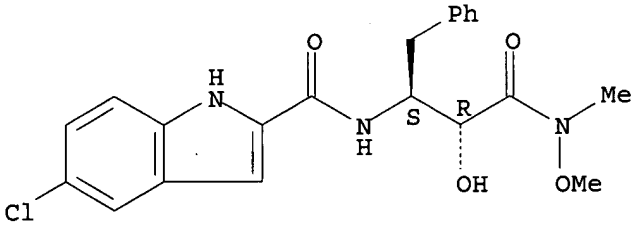
RN 186392-40-5 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



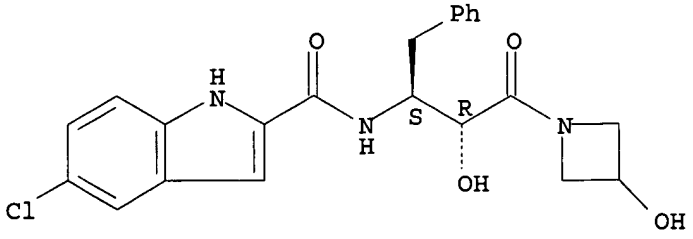
RN 186392-43-8 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186392-46-1 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(3-hydroxy-1-azetidinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

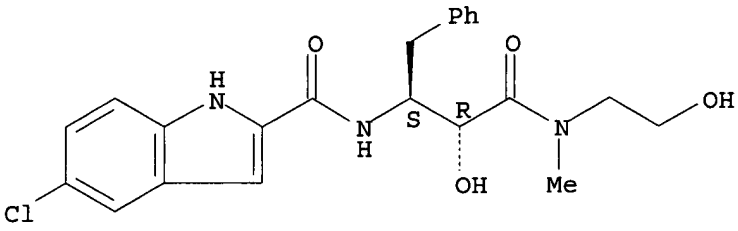
Absolute stereochemistry.



RN 186392-49-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(2-

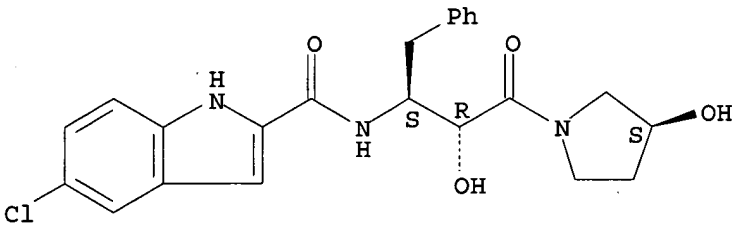
hydroxyethyl)methylamino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



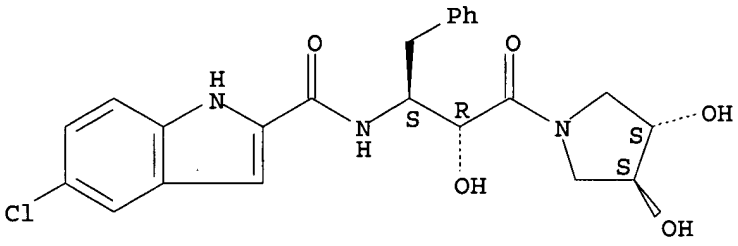
RN 186392-53-0 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(3S)-3-hydroxy-1-pyrrolidinyl]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

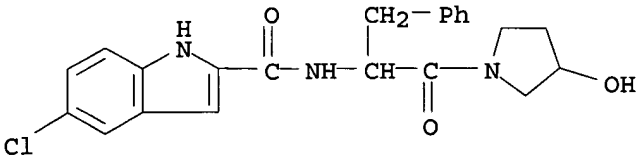


RN 186392-64-3 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

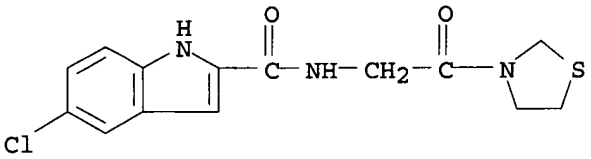
Absolute stereochemistry.



RN 186429-66-3 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-(3-hydroxy-1-pyrrolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

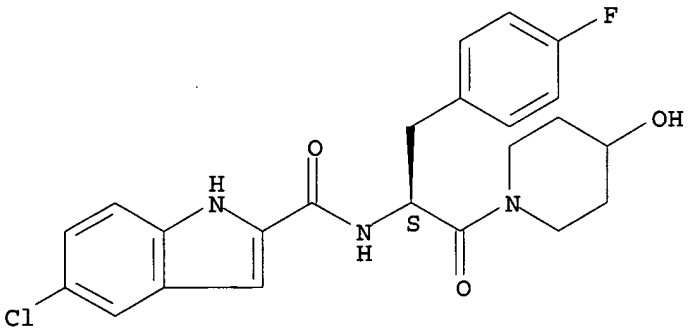


RN 186430-04-6 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-oxo-2-(3-thiazolidinyl)ethyl]- (9CI) (CA INDEX NAME)



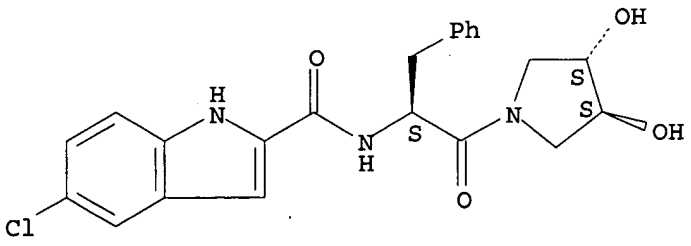
RN 186430-23-9 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186430-40-0 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

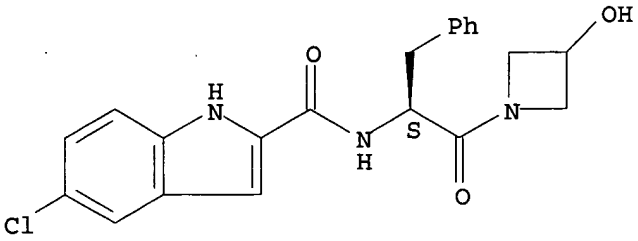
Absolute stereochemistry.



RN 186431-27-6 HCAPLUS

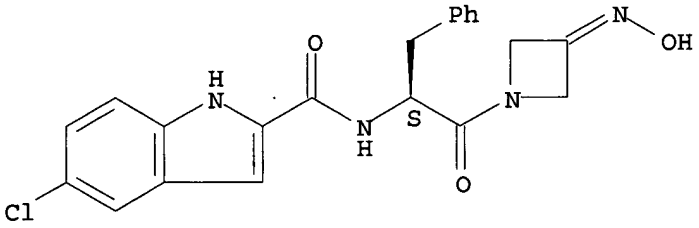
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-azetidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



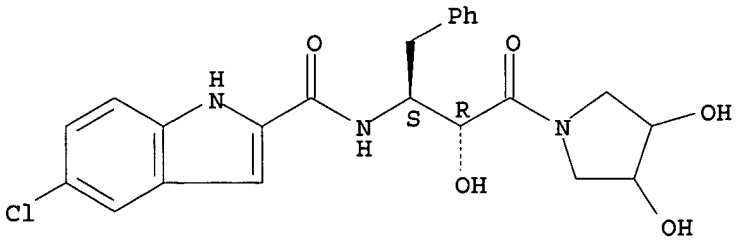
RN 186431-28-7 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[3-(hydroxyimino)-1-azetidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



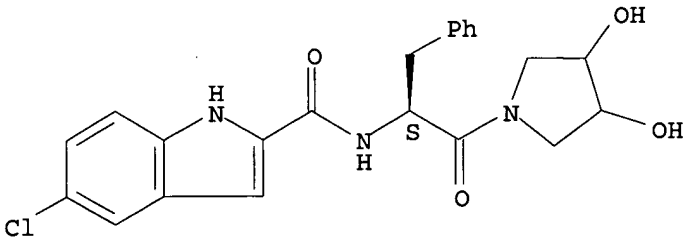
RN 208830-24-4 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(3,4-dihydroxy-1-pyrrolidinyl)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 208830-25-5 HCAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3,4-dihydroxy-1-pyrrolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9035-74-9**, Glycogen phosphorylase
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(use of glycogen phosphorylase **inhibitor** for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)
RN 9035-74-9 HCAPLUS
CN Phosphorylase (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L31 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:197402 HCAPLUS
DOCUMENT NUMBER: 128:275085
TITLE: Combination therapy for reducing the risks associated with **cardiovascular** disease
INVENTOR(S): Gould, Robert J.; Nichtberger, Steven A.; Rhymer, Patricia A.; Olofsson, Lars
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Gould, Robert J.; Nichtberger, Steven A.; Rhymer, Patricia A.; Olofsson, Lars
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811896	A1	19980326	WO 1997-US16388	19970915
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9743508	A1	19980414	AU 1997-43508	19970915
AU 723315	B2	20000824		
EP 946178	A1	19991006	EP 1997-941644	19970915
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001500875	T2	20010123	JP 1998-514815	19970915
US 6251852	B1	20010626	US 1997-929595	19970915
US 6235706	B1	20010522	US 1999-147858	19990527
US 2001036913	A1	20011101	US 2001-764511	20010118
US 6403571	B2	20020611		

PRIORITY APPLN. INFO.:			
US 1996-26581P	P	19960918	
GB 1996-21970	A	19961022	
WO 1997-US16388	W	19970915	

US 1999-147858 A3 19990527

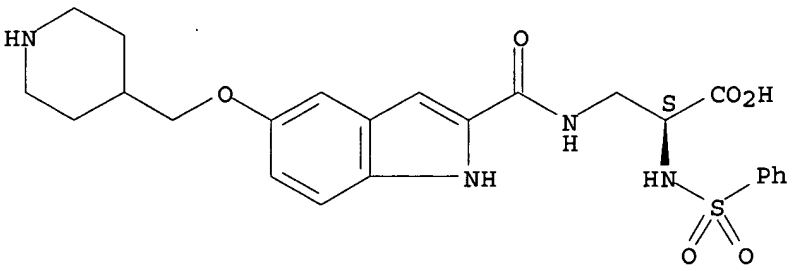
AB The instant invention involves a combination therapy and pharmaceutical compns. comprised of a therapeutically effective amt. of a cholesterol reducing agent such as an HMG-CoA reductase inhibitor in combination with a platelet aggregation inhibitor which is useful for inhibiting platelet aggregation, for inhibiting the formation of thrombotic occlusions, and for treating, preventing and reducing the risk of occurrence of **cardiovascular** and cerebrovascular events and related vaso-occlusive disorders. Tablets were prepd. contg. simvastatin and a glycoprotein IIb/IIIa receptor antagonist.

IT **190261-01-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy for reducing the risks assocd. with cardiovascular disease)

RN 190261-01-9 HCAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[[5-(4-piperidinylmethoxy)-1H-indol-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:121995 HCAPLUS

DOCUMENT NUMBER: 128:252809

TITLE: Discovery of a human liver **glycogen phosphorylase inhibitor** that lowers blood glucose in vivo

AUTHOR(S): Martin, William H.; Hoover, Dennis J.; Armento, Sandra J.; Stock, Ingrid A.; Mcpherson, R. Kirk; Danley, Dennis E.; Stevenson, Ralph W.; Barrett, Eugene J.; Treadway, Judith L.

CORPORATE SOURCE: Central Research Division, Department of Exploratory Medicinal Biology, Pfizer, Inc, Groton, CT, 06340, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(4), 1776-1781
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An **inhibitor** of human liver **glycogen phosphorylase** a (HLGPa) has been identified and characterized in vitro and in vivo. This substance, [R-(R*,S*)]-5-chloro-N-[3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-1H-indole-2-carboxamide (CP-91149), inhibited HLGPa with an IC50 of 0.13 .mu.M in the presence of 7.5 mM glucose. CP-91149 resembles caffeine, a known allosteric phosphorylase inhibitor, in that it is 5- to 10-fold less potent in the absence of glucose. Further anal., however, suggests that CP-91149 and caffeine are kinetically distinct. Functionally, CP-91149

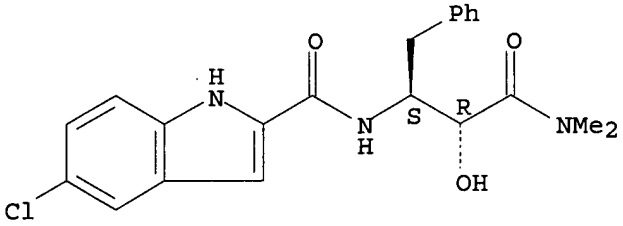
inhibited glucagon-stimulated glycogenolysis in isolated rat hepatocytes ($P < 0.05$ at 10-100 .mu.M) and in primary human hepatocytes (2.1 .mu.M IC50). In vivo, oral administration of CP-91149 to **diabetic** ob/ob mice at 25-50 mg/kg resulted in rapid (3 h) glucose lowering by 100-120 mg/dL ($P < 0.001$) without producing hypoglycemia. Further, CP-91149 treatment did not lower glucose levels in normoglycemic, nondiabetic mice. In ob/ob mice pretreated with 14C-glucose to label liver glycogen, CP-91149 administration reduced 14C-glycogen breakdown, confirming that glucose lowering resulted from inhibition of glycogenolysis in vivo. These findings support the use of CP-91149 in investigating glycogenolytic vs. gluconeogenic flux in hepatic glucose prodn., and they demonstrate that glycogenolysis inhibitors may be useful in the treatment of type 2 **diabetes**.

IT **186392-40-5P**, CP 91149
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(blood glucose lowering by CP-91149, oral inhibitor of human liver glycogen phosphorylase, in model of type II diabetes)

RN 186392-40-5 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

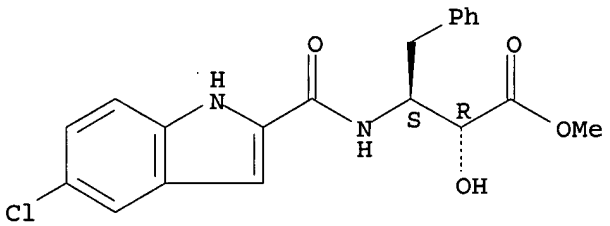


IT **186392-22-3P 186392-32-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(blood glucose lowering by CP-91149, oral inhibitor of human liver glycogen phosphorylase, in model of type II diabetes)

RN 186392-22-3 HCAPLUS

CN Benzenebutanoic acid, .beta.-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-.alpha.-hydroxy-, methyl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

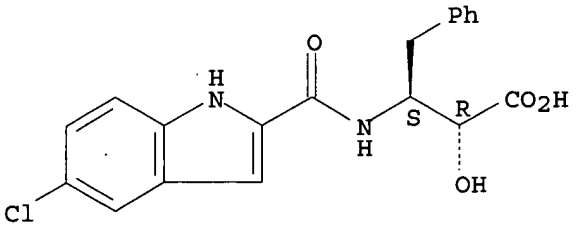
Absolute stereochemistry.



RN 186392-32-5 HCAPLUS

CN Benzenebutanoic acid, .beta.-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-.alpha.-hydroxy-, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

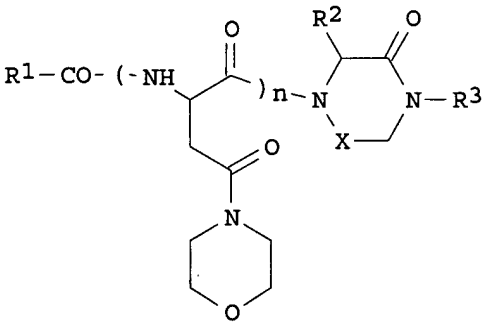
Absolute stereochemistry.



L31 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:115888 HCAPLUS
DOCUMENT NUMBER: 128:230390
TITLE: Preparation of piperazine derivatives as NO producing inhibitors
INVENTOR(S): Ito, Yoshikuni; Yatabe, Isao; Inoue, Takayuki; Hamashima, Hitoshi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10045751	A2	19980217	JP 1997-131796	19970522

PRIORITY APPLN. INFO.: AU 1996-83 19960527
OTHER SOURCE(S): MARPAT 128:230390
GI



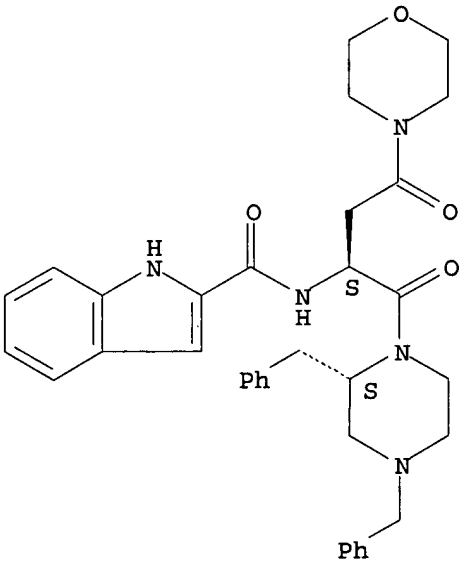
I

AB The title compds. [I; R1 = indolyl, benzofuranyl; R2, R3 = (un)substituted alkyl, aryl, etc.; X = CH2, CO; n = 0, 1] are prepd. I, possessing NO producing inhibitory activity, are useful for prevention and treatment of brain infarction, Alzheimer disease, **heart** failure, **diabetes** and related diseases. Thus, (S)-I (R1 = 2-indolyl, R2 = CH2C6H5, R3 = Me, X = CH2, n = 1) is prepd. and showed 70.9% inhibitory activity at 10-5 M for mouse RAW264.7 cell.
IT **204328-01-8P 204328-04-1P 204328-07-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperazine derivs. as NO producing inhibitors)

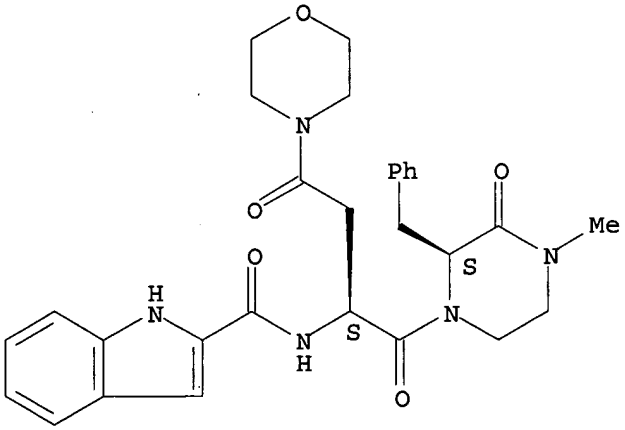
RN 204328-01-8 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[[2,4-bis(phenylmethyl)-1-piperazinyl]carbonyl]-3-(4-morpholinyl)-3-oxopropyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



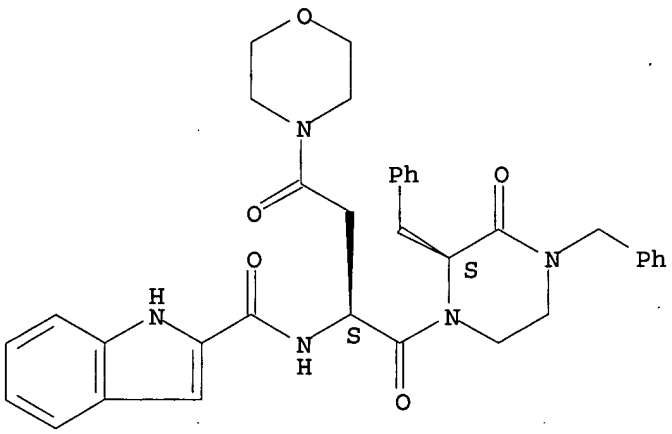
RN 204328-04-1 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[[4-methyl-3-oxo-2-(phenylmethyl)-1-piperazinyl]carbonyl]-3-(4-morpholinyl)-3-oxopropyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 204328-07-4 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[3-(4-morpholinyl)-3-oxo-1-[[3-oxo-2,4-bis(phenylmethyl)-1-piperazinyl]carbonyl]propyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

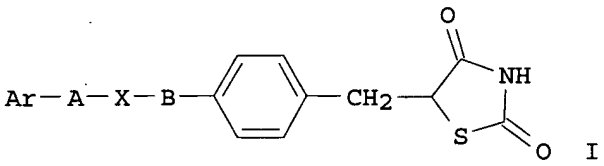
Absolute stereochemistry.



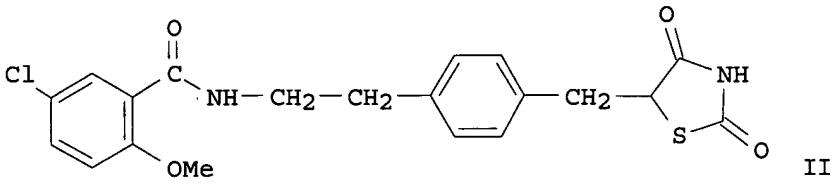
L31 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:275069 HCAPLUS
DOCUMENT NUMBER: 125:10799
TITLE: Thiazolidinedione compounds useful for treating conditions of insulin-resistance and/or non insulin-dependent **diabetes**
INVENTOR(S): Regnier, Gilbert; Charton, Yves; Duhault, Jacques; Espinal, Joseph
PATENT ASSIGNEE(S): ADIR et Compagnie, Fr.
SOURCE: U.S., 6 pp., Cont.-in-part of U.S. Ser. No. 133,898, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5506245	A	19960409	US 1995-374970	19950119
FR 2696743	A1	19940415	FR 1992-12123	19921012
FR 2696743	B1	19941223		

PRIORITY APPLN. INFO.: FR 1992-12123 19921012
US 1993-133898 19931012
OTHER SOURCE(S): MARPAT 125:10799
GI



I



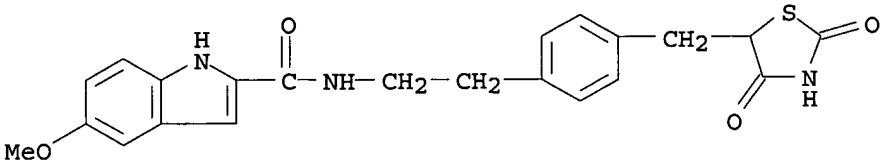
II

AB Thiazolidinedione compds. I useful for treating conditions of insulin-resistance and/or non insulin-dependent **diabetes** are provided, wherein: Ar represents a polymethylene ring, a mono-, bi- or tricyclic hydrocarbon radical, or a mono-, bi- or tri-cyclic heterocyclic radical contg. 1 or 2 hereto atoms selected from nitrogen, oxygen and sulfur atoms; A represents, e.g., a single bond, a hydrocarbon chain having 2 or 3 carbon atoms and including a double bond, or a chain of the formula (CH2)m , O(CH2)m or S(CH2)m wherein: m is an integer from 1 to 3; X represents an oxygen atom, CONR or SO2NR wherein R represents a hydrogen atom or a straight-chain or branched alkyl radical having from 1 to 5 carbon atoms and optionally including a double bond, or, when A represents a single bond and Ar represents a Ph radical, R may also represent a carbonyl radical bonded to Ar by its free bond such that Ar-A-X together form a phthalimido radical; B represents a satd. hydrocarbon chain having from 1 to 6 carbon atoms which is optionally branched and/or substituted by a hydroxy radical or an oxo radical. Thus, e.g., cyclization of Me 3-{4-[2-(2-methoxy-5-chlorobenzamido)ethyl]phenyl}-2-chloropropionate with thiourea afforded 5-{4-[2-(2-methoxy-5-chlorobenzamido)ethyl]benzyl}thiazolidine-2,4-dione II which exhibited the same hypoglycemic effect at .ltoreq.10 mg/kg/day for 4 days as Ciglitazone at 50-100 mg/kg/day for 4 days. The compds. of the invention do not have any influence on the level of circulating glucose but decrease the level of triglycerides and free fatty acids in the plasma and also the level of immuno-reactive insulin.

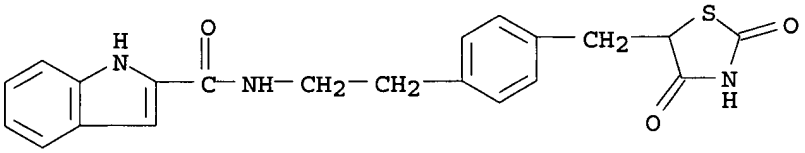
IT **174772-17-9P 174772-25-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(thiazolidinedione compds. useful for treating conditions of insulin-resistance and/or non insulin-dependent diabetes)

RN 174772-17-9 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethyl]-5-methoxy- (9CI) (CA INDEX NAME)



RN 174772-25-9 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethyl]- (9CI) (CA INDEX NAME)

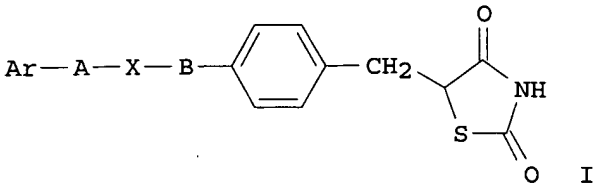


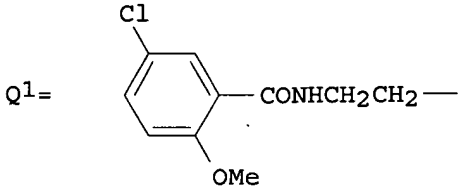
L31 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:58393 HCAPLUS
DOCUMENT NUMBER: 124:232440
TITLE: Thazolidinedione compounds useful as antidiabetics
INVENTOR(S): Regnier, Gilbert; Charton, Yves; Duhault, Jacques; Espinal, Joseph
PATENT ASSIGNEE(S): Adir et Compagnie, Fr.
SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 133,898, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5478853	A	19951226	US 1995-376052	19950120
FR 2696743	A1	19940415	FR 1992-12123	19921012
FR 2696743	B1	19941223		

PRIORITY APPLN. INFO.: FR 1992-12123 19921012
US 1993-133898 19931012

OTHER SOURCE(S): MARPAT 124:232440
GI

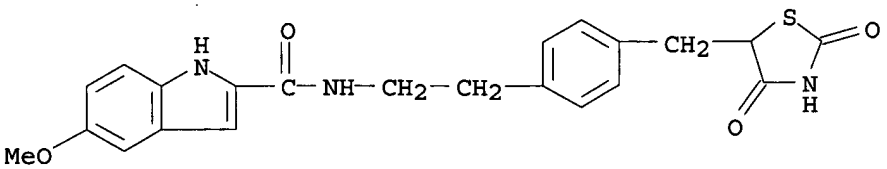




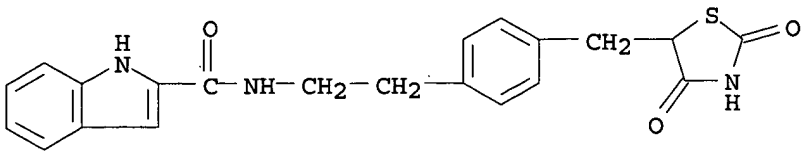
AB The title compds. are 5-(4-substituted benzyl)thiazolidine-2,4-diones I [Ar = polymethylene ring with optional alkyl substituent(s), (un)substituted aryl or heterocyclyl; A = bond, hydrocarbondiyl with double bond, (CH2)1-3, CMe2(CH2)0-2, (un)substituted CHPh(CH2)0-2, O(CH2)1-3, S(CH2)1-3; X = O, CONR, SO2NR; R = H, alkyl, alkenyl; or ArAX = phthalimido; B = satd. hydrocarbondiyl with optional OH or oxo substituent] and their enantiomers, diastereoisomers, and pharmaceutically tolerable salts. The compds. are useful for treating insulin resistance and/or non-insulin-dependent **diabetes**, possibly assocd. with hypertension. An exemplary compd. compd. is 5-[4-[2-(2-methoxy-5-chlorobenzamido)ethyl]benzyl]thiazolidine-2,4-dione, i.e., I [Ar-A-X-B- = Q1] (II), which was prepd. by cyclization of the corresponding 3-phenyl-2-chloropropionic acid deriv. with thiourea in sulfolane at 120.degree., followed by hydrolysis with aq. HCl at 100.degree.. II, at .ltoreq. 10 mg/kg/day orally in mice, had the same hypoglycemic effect as ciglitazone at 50-100 mg/kg/day. II also had little or no hematol. effect at 250 mg/kg/day in rats, whereas pioglitazone had strong adverse effects at 100 mg/kg/day.

IT **174772-17-9P 174772-25-9P**
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of thiazolidinediones as antidiabetics)

RN 174772-17-9 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethyl]-5-methoxy- (9CI) (CA INDEX NAME)



RN 174772-25-9 HCAPLUS
CN 1H-Indole-2-carboxamide, N-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethyl]- (9CI) (CA INDEX NAME)



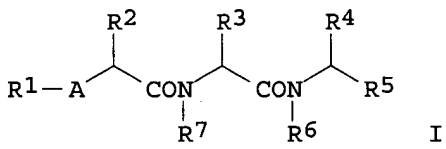
L31 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:410003 HCAPLUS
DOCUMENT NUMBER: 121:10003
TITLE: Preparation of peptides by reaction of olefinic alcohol and enol ether for treatment of tachypnea and **myocardial reperfusion** injury.
INVENTOR(S): Itsumi, Keiji; Kei, Seihaku; Fukami, Jikiki; Hashihon, Sanashi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 131 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05208914	A2	19930820	JP 1992-233604	19920901
US 5430022	A	19950704	US 1993-86094	19930706
US 5656604	A	19970812	US 1995-422944	19950417

PRIORITY APPLN. INFO.:

US 1991-753997	19910903
GB 1990-10740	19900514
GB 1990-26254	19901203
GB 1991-4064	19910227
US 1991-696701	19910507
US 1992-845056	19920303
US 1993-86094	19930706

OTHER SOURCE(S): MARPAT 121:10003
GI



I

AB Title compds. I [R1 = H, acyl; R2 = alkyl, (un)substituted aralkyl, cycloalkylalkyl, (un)substituted heterocyclylalkyl; R3 = (un)substituted heterocyclylalkyl, (un)substituted aralkyl; R4 = H, (un)substituted alkyl; R5 = carboxy, (un)protected carboxy, (un)protected carboxyalkyl; R6 = H, (un)substituted alkyl; R7 = H, alkyl; A = O, NH, alkylimino, alkylene; with provisos], useful for the treatment of many **cardiovascular** injury, e.g., hypertension, are prepd. Thus, a mixt. of N-phenylacetyl-Leu-OH and H-D-Trp(Me)-D-Phe-OMe.HCl in DMF was stirred with ice cooling for 4.5 h to give PhCH2CO-Leu-D-Trp(Me)-D-Phe-OMe. In an in vitro study, Q-Leu-D-Trp(Me)-D-Pya-OH.HCl [Q = cyclohexylcarbamoyl, Pya = 2-pyridylalanine] (also prepd.) had an IC50 of 2.3.times.10-9 M against

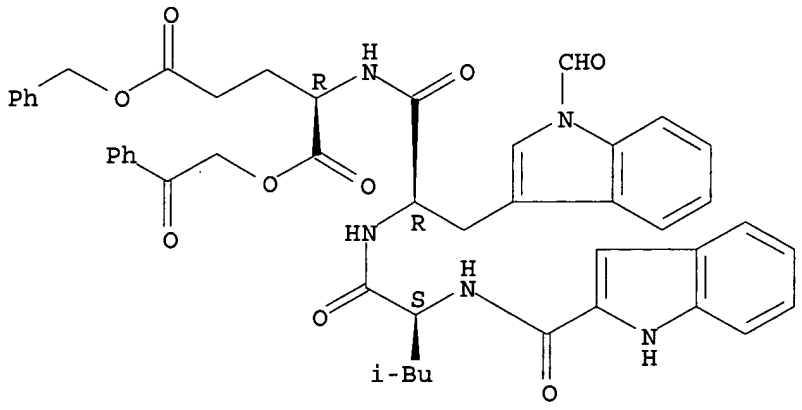
the binding of 125-I-endothelin-1 with pig aorta receptors.

IT **142377-52-4P 142378-01-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, for treatment of tachypnea and myocardial reperfusion injury)

RN 142377-52-4 HCAPLUS

CN D-Glutamic acid, N-[1-formyl-N-[N-(1H-indol-2-ylcarbonyl)-L-leucyl]-D-tryptophyl]-, 1-(2-oxo-2-phenylethyl) 5-(phenylmethyl) ester (9CI) (CA INDEX NAME)

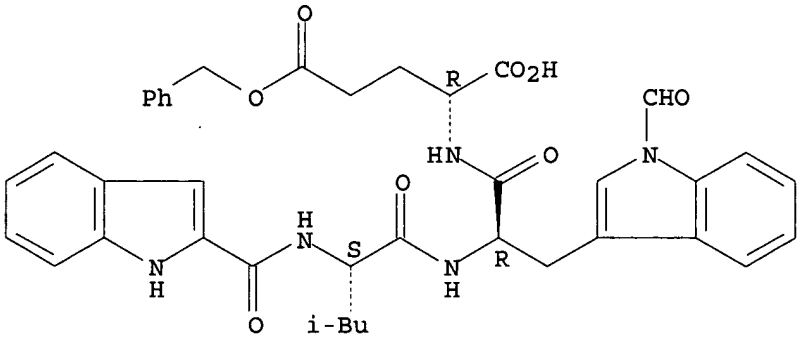
Absolute stereochemistry.



RN 142378-01-6 HCAPLUS

CN D-Glutamic acid, N-[1-formyl-N-[N-(1H-indol-2-ylcarbonyl)-L-leucyl]-D-tryptophyl]-, 5-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:409168 HCAPLUS

DOCUMENT NUMBER: 119:9168

TITLE: Preparation of oxiranyl and oxetanyl renin inhibiting compounds

INVENTOR(S): Rosenberg, Saul H.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

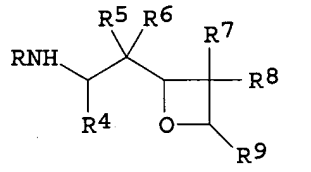
SOURCE: PCT Int. Appl., 168 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

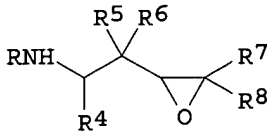
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9222313	A1	19921223	WO 1992-US4423	19920526
W: AU, CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
US 5258362	A	19931102	US 1992-880250	19920513
AU 9221593	A1	19930112	AU 1992-21593	19920526

PRIORITY APPLN. INFO.: US 1991-713475 19910611
US 1992-880250 19920513
WO 1992-US4423 19920526

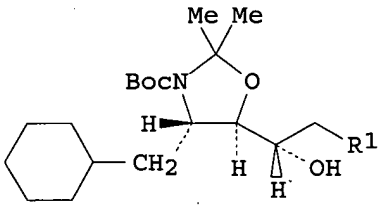
OTHER SOURCE(S): MARPAT 119:9168
GI



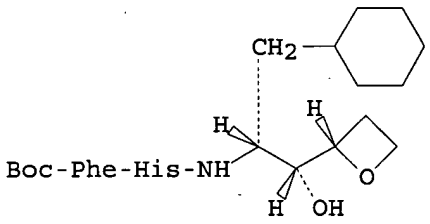
I



II



III

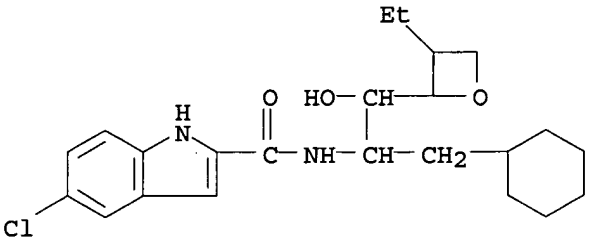


V

AB The title compds. I and II [R = mimic of Phe-His dipeptide; R4 = lower alkyl, cycloalkyl, arylalkyl; R5 = H, lower alkyl, hydroxyalkyl, lower alkenyl, CHO; R6 = OH, NH2; R7 = H, lower alkyl; R8 = H, lower alkyl, hydroxyalkyl, alkoxyalkyl, alkoxyalkyl, thioalkoxyalkyl, haloalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, cycloalkyl, cycloalkylalkyl, lower alkenyl, alkynyl, aryl, arylalkyl, heterocyclic, heterocycloalkyl; R7R8 = (CH2)n, n = 3-6; R9 = lower alkyl] or a pharmaceutically acceptable salt, ester, or prodrug of, were prepd. as renin inhibitors. Thus, Reformatskii reaction of (4S,5R)-3-tert-butoxycarbonyl-4-cyclohexylmethyl-2,2-dimethyloxazolidine-5-carboxaldehyde with benzyl bromoacetate gave hydroxy ester III (Boc = Me3CO2C; R1 = CO2CH2Ph), which was reduced with NaBH4-CaCl2 to diol III (R1 = CH2OH) and selectively tosylated to tosylate III (R1 = CH2O3SC6H4Me-4) (IV). Cyclization of tosylate IV to the corresponding oxetane, followed by acidic deprotection, coupling with Boc-Phe-His(Boc)-OH, and selective deblocking gave oxetanyl peptide V. Compds. I and II are useful in treating hypertension, congestive **heart** failure, glaucoma, and inhibiting HIV-1 and HIV-2 proteases.

IT **147896-46-6P**
RL: **BAC (Biological activity or effector, except adverse)**; SPN

(Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as renin inhibitor)
RN 147896-46-6 HCAPLUS
CN L-Altritol, 4,6-anhydro-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-1-cyclohexyl-1,2,5-trideoxy-5-ethyl- (9CI) (CA INDEX NAME)



L31 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:493611 HCAPLUS
DOCUMENT NUMBER: 109:93611
TITLE: Preparation and testing of (aminopropoxy)naphthylcarboxamidopentylalanylprolines and indole analogs as **cardiovascular** agents
INVENTOR(S): Allan, Geoffrey; Hardy, George William; Bull, Donald; Mills, Gail; Lee, Grahame Roy
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Eur. Pat. Appl., 43 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

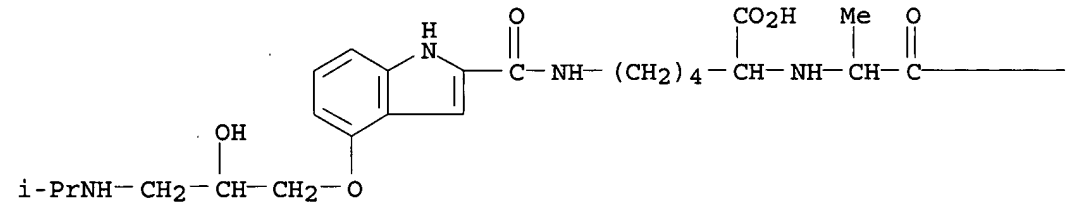
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 234946	A2	19870902	EP 1987-301740	19870227
EP 234946	A3	19880817		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FI 8700872	A	19870829	FI 1987-872	19870227
DK 8701033	A	19870829	DK 1987-1033	19870227
AU 8769536	A1	19870903	AU 1987-69536	19870227
JP 62252799	A2	19871104	JP 1987-45119	19870227
HU 46045	A2	19880928	HU 1987-816	19870227
ZA 8701454	A	19881026	ZA 1987-1454	19870227
DD 263052	A5	19881221	DD 1987-300269	19870227
PRIORITY APPLN. INFO.:			GB 1986-5049	19860228
			GB 1986-20767	19860828

AB Me2CHNHCH2CH(OH)CH2OXCONH(CH2)4CHZNHCHMeCOY (I; X = naphthyl, indolyl ring system; Y = CO2H, C2-5 alkoxycarbonyl; Z = carboxypyrrolidinyl) were prepd. as antihypertensives. Me 4-hydroxyindole-2-carboxylate (prepn. given) was treated with NaH in DMF and 2S-glycidyl tosylate was added at 0.degree.. The mixt. was stirred 3 h at 50.degree. to give the 4-oxiranylmethoxy compd., which was heated with Me2CHNH2 in DMF/H2O to give Me 4-[2(S)-hydroxy-3-isopropylamino]-1H-indole-2-carboxylate. The latter was N-protected, sapond., coupled with tert-Bu N-[1(S)-tert-butoxycarbonyl-5-aminopentyl]-(S)alanyl-(S)-prolinate (prepn. given) to give N-1S-carboxy-5-[4-(2S-hydroxy-3-isopropylaminopropoxy)-1H-indol-2-ylcarboxamido]pentyl-S-alanyl-S-proline. The latter inhibited ACE in a

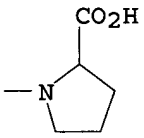
test of angiotensin-I-induced pig ileum contractility with an EC50 of 1.4 nM.

IT **115794-86-0P**
RL: **BAC (Biological activity or effector, except adverse)**; SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as cardiovascular agent)
RN 115794-86-0 HCAPLUS
CN L-Proline, N-[(1S)-1-carboxy-5-[[[4-[(2S)-2-hydroxy-3-[(1-methylethyl)amino]propoxy]-1H-indol-2-yl]carbonyl]amino]pentyl]-L-alanyl- (9CI) (CA INDEX NAME)

PAGE 1-A

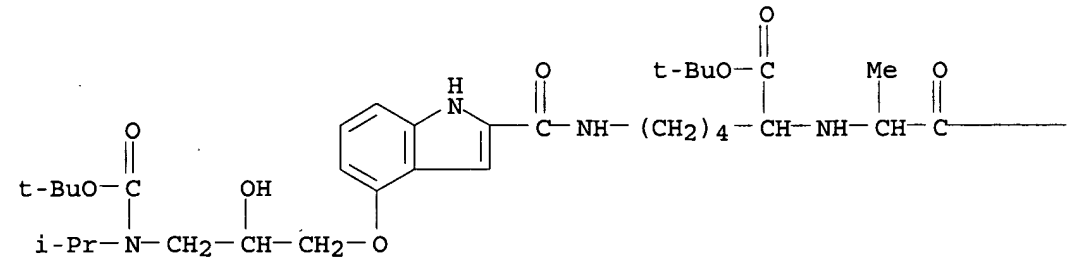


PAGE 1-B



IT **115794-89-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for cardiovascular agent)
RN 115794-89-3 HCAPLUS
CN L-Proline, 1-[N-[1-[(1,1-dimethylethoxy)carbonyl]-5-[[[4-[3-[[(1,1-dimethylethoxy)carbonyl](1-methylethyl)amino]-2-hydroxypropoxy]-1H-indol-2-yl]carbonyl]amino]pentyl]-L-alanyl]-, 1,1-dimethylethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B